

identified as AA027096 (zk04d03.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 469541 3'), AA027135 (zk04d03.r1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 469541 5'), AA166312 (ms42g11.r1 Life Tech mouse embryo 135dpc 10666014 Mus musculus cDNA clone 614276 5' similar to TRE238793 E238793 DUALIN), AA535890 (nf94a03.s1 NCI_CGAP_Co3 Homo sapiens cDNA clone IMAGE:927532), H14467 (yl25g07.r1 Homo sapiens cDNA clone 159324 5' similar to contains HGR repetitive element), T21281 (Human gene signature HUMGS02637), T61016 (Total DNA sequence from cosmid clones LP(2)127 and LP(2)128), U47621 (Human nucleolar autoantigen No55 mRNA, complete cds), W51808 (zc48g04.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 325590 5' similar to PIR:S20742 S20742 synaptonemal complex protein Sc65 - rat; contains Alu repetitive element; mRNA sequence), and X97607 (G.gallus mRNA for cartilage associated protein). The predicted amino acid sequence disclosed herein for bd306_7 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted bd306_7 protein demonstrated at least some similarity to sequences identified as R95913 (Neural thread protein [Homo sapiens]), U47621 (nucleolar autoantigen No55 [Homo sapiens]), and X97607 (cartilage associated protein [Gallus gallus]). Two regions of bd306_7 protein (amino acids 148-217 and 298-367 of SEQ ID NO:2) align with the same region, amino acids 145-214, of cartilage associated protein. The homology between bd306_7 protein and nucleolar autoantigen No55 is also good, but in this case it appears that bd306_7 amino acids 148-189 is similar to two regions of No55 (amino acids 145-186 and 296-337), and bd306_7 amino acids 298-367 are also similar to nearly the same two regions of No55 (amino acids 145-214 and 296-365). This implies that two regions in bd306_7 (roughly 148-189 and 298-367) are similar to each other, and one copy of this region is found in cartilage associated protein, but both are present in No55. Cartilage associated protein is reported to be localized to the extracellular matrix [J. Cell Sci 1997 110(Pt 12):1351-1359], while No55 is found in the granular component of the nucleolus [Mol Biol Cell 1996 7(7):1015-1024]. Based upon sequence similarity, bd306_7 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of bd306_7 also indicates that it may contain an Alu repetitive element.

bd306_7 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 52 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "fj283_11" and Clone "fj283_6"

Polynucleotides of the present invention have been identified as clone "fj283_11" and clone "fj283_6". fj283_11 and fj283_6 were isolated from a human adult lung carcinoma cDNA library using methods which are selective for cDNAs encoding secreted
5 proteins (see U.S. Pat. No. 5,536,637), or were identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. fj283_11 and fj283_6 are full-length clones, including the entire coding sequence of a secreted protein (also referred to herein as "fj283 protein").

The nucleotide sequence of fj283_11 as presently determined is reported in SEQ
10 ID NO:3, and includes a poly(A) tail. The nucleotide sequence of fj283_6 as presently determined is reported in SEQ ID NO:198, and includes a poly(A) tail. Although cDNA clones fj283_11 and fj283_6 have different nucleotide sequences, perhaps as a result of alternative splicing of a common primary mRNA transcript (particularly between nucleotide 402 and nucleotide 618 of SEQ ID NO:198), these clones are predicted to
15 encode the same protein. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the fj283 protein corresponding to the foregoing nucleotide sequences is reported in SEQ ID NO:4. Amino acids 8 to 20 of SEQ ID NO:4 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 21. Due to the hydrophobic nature of the predicted
20 leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the fj283 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone fj283_11 should be approximately 3350 bp. The EcoRI/NotI restriction fragment
25 obtainable from the deposit containing clone fj283_6 should be approximately 2700 bp.

The nucleotide sequences disclosed herein for fj283_11 and fj283_6 were searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. fj283_11 and/or fj283_6 demonstrated at least some similarity with sequences identified as AA052962 (zl70c02.s1 Stratagene
30 colon (#937204) Homo sapiens cDNA clone 509954 3' similar to gb D14531 60S RIBOSOMAL PROTEIN L9 (HUMAN)), AA080949 (zn04d12.r1 Stratagene hNT), AA160948 (zq40e12.r1 Stratagene hNT neuron (#937233) Homo sapiens cDNA clone 632206 5'), AA195089 (zr34c02.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 665282

5', mRNA sequence), AA258887 (zs32b02.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:686859 5'), H97993 (yw06e03.s1 Homo sapiens cDNA clone 251452 3'), R19768 (yg40g06.r1 Homo sapiens cDNA clone 34951 5'), U09953 (Human ribosomal protein L9 mRNA, complete cds), Z73639 (Human DNA sequence from cosmid V389H8 on chromosome X; Contains mRNA near btk gene involved in a-gamma-globulinemia, ESTs, STS), and Z73901 (Human DNA sequence from cosmid V389H8, between markers DXS366 and DXS87 on chromosome X contains pseudogene, mRNA near btk gene involved in a-gamma-globulinemia, ESTs, STS). The predicted amino acid sequence disclosed herein for the fj283 protein was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted fj283 protein demonstrated at least some similarity to sequences identified as AB011084 (KIAA0512 protein [Homo sapiens]) and U09953 (ribosomal protein L9 [Homo sapiens]). Based upon sequence similarity, fj283 proteins and each similar protein or peptide may share at least some activity. Profile hidden markov model analysis has revealed the presence of an Armadillo/beta-catenin-like domain within the predicted fj283 protein sequence. The armadillo multigene family comprises many proteins widely differing in sizes and functions which have in common a variable number of tandemly repeated arm sequences of about 42 amino acids in length. Many, but not all, armadillo-repeat-containing proteins are nuclear in localization. The predicted fj283 protein does not appear to be of the nuclear variety, but rather appears to be an extracellular protein.

Clone "fk317_3"

A polynucleotide of the present invention has been identified as clone "fk317_3". fk317_3 was isolated from a human adult kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. fk317_3 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "fk317_3 protein").

The nucleotide sequence of fk317_3 as presently determined is reported in SEQ ID NO:5, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the fk317_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:6.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone fk317_3 should be approximately 1400 bp.

The nucleotide sequence disclosed herein for fk317_3 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
5 FASTA search protocols. fk317_3 demonstrated at least some similarity with sequences identified as AA568588 (nm21b11.s1 NCI_CGAP_Co10 Homo sapiens cDNA clone IMAGE:1060797), AC002326 (Genomic sequence from Human 6, complete sequence), H48562 (yq78g07.s1 Homo sapiens cDNA clone 201948 3' similar to contains Alu repetitive element; contains MER30 repetitive element), T67164 (Human alpha-N-
10 acetylglucosaminidase gene), and Z46941 (H.sapiens DNA for alu repeats). The predicted amino acid sequence disclosed herein for fk317_3 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted fk317_3 protein demonstrated at least some similarity to sequences identified as X55777 (put. ORF [Homo sapiens]). Based upon sequence similarity, fk317_3 proteins
15 and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the fk317_3 protein sequence centered around amino acid 42 of SEQ ID NO:6. The nucleotide sequence of fk317_3 indicates that it may contain an Alu repetitive element.

20 Clone "k213_2x"

A polynucleotide of the present invention has been identified as clone "k213_2x". Secreted cDNA clones were first isolated from a murine adult bone marrow (stromal cell line FCM-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or were identified as encoding a secreted
25 or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. These murine cDNAs were then used to isolate k213_2x, a full-length human cDNA clone, including the entire coding sequence of a secreted protein (also referred to herein as "k213_2x protein").

The nucleotide sequence of k213_2x as presently determined is reported in SEQ
30 ID NO:7, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the k213_2x protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:8. Amino acids 26 to 38 are a predicted leader/signal sequence, with the predicted mature amino

acid sequence beginning at amino acid 39. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the k213_2x protein.

5 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone k213_2x should be approximately 1900 bp.

 The nucleotide sequence disclosed herein for k213_2x was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. k213_2x demonstrated at least some similarity with sequences
10 identified as AA123852 (mp96e08.r1 Soares 2NbMT Mus musculus cDNA clone 577094 5'), AA362005 (EST71348 T-cell lymphoma Homo sapiens cDNA 5' end), AA436477 (zv08f05.s1 Soares NhHMPu S1 Homo sapiens cDNA clone 753057 3'), AA436528 (zv08f05.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 753057 5'), AA643506 (nq86f04.s1 NCI_CGAP_Co9 Homo sapiens cDNA clone IMAGE:1159231, mRNA
15 sequence), F13485 (H. sapiens partial cDNA sequence; clone c-3dh08), and T19502 (Human gene signature HUMGS00560). Based upon sequence similarity, k213_2x proteins and each similar protein or peptide may share at least some activity.

 k213_2x protein was expressed in a COS cell expression system, and an expressed protein band of approximately 6 kDa was detected in membrane fractions using SDS
20 polyacrylamide gel electrophoresis.

Clone "na316_1"

 A polynucleotide of the present invention has been identified as clone "na316_1". na316_1 was isolated from a human adult brain (corpus callosum) cDNA library using
25 methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. na316_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na316_1 protein").

30 The nucleotide sequence of na316_1 as presently determined is reported in SEQ ID NO:9, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the na316_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:10. Amino

acids 30 to 42 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 43. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na316_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na316_1 should be approximately 900 bp.

The nucleotide sequence disclosed herein for na316_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No hits were found in the database. The TopPredII computer program predicts two potential transmembrane domains within the na316_1 protein sequence, centered around amino acids 31 and 66 of SEQ ID NO:10, respectively.

Clone "nf93_20"

A polynucleotide of the present invention has been identified as clone "nf93_20". nf93_20 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nf93_20 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nf93_20 protein").

The nucleotide sequence of nf93_20 as presently determined is reported in SEQ ID NO:11, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nf93_20 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:12. Amino acids 6 to 18 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 19. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nf93_20 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nf93_20 should be approximately 2000 bp.

The nucleotide sequence disclosed herein for nf93_20 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nf93_20 demonstrated at least some similarity with sequences identified as AA063620 (ze87g07.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 366012 3'), AA317410 (EST19337 Retina II Homo sapiens cDNA 5' end), H29417 (ym60e07.r1 Homo sapiens cDNA clone 52631 5'), and N41425 (yw93e08.r1 Homo sapiens cDNA clone 259814 5'). Based upon sequence similarity, nf93_20 proteins and each similar protein or peptide may share at least some activity.

nf93_20 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 29 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "np164_1"

A polynucleotide of the present invention has been identified as clone "np164_1". np164_1 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. np164_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "np164_1 protein").

The nucleotide sequence of np164_1 as presently determined is reported in SEQ ID NO:13, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the np164_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:14. Amino acids 348 to 360 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 361. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the np164_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone np164_1 should be approximately 2100 bp.

The nucleotide sequence disclosed herein for np164_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and

FASTA search protocols. np164_1 demonstrated at least some similarity with sequences identified as N63143 (yz37c12.s1 Homo sapiens cDNA clone 285238 3'), T19992 (Human gene signature HUMGS01129), Z46676 (Caenorhabditis elegans cosmid C08B11, complete sequence), and Z74910 (S.cerevisiae chromosome XV reading frame ORF YOR002w). The
5 predicted amino acid sequence disclosed herein for np164_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted np164_1 protein demonstrated at least some similarity to sequences identified as Z46676 (C08B11.8 [Caenorhabditis elegans]) and Z74910 (ORF YOR002w [Saccharomyces cerevisiae]). Based upon sequence similarity, np164_1 proteins and each
10 similar protein or peptide may share at least some activity. The TopPredII computer program predicts ten potential transmembrane domains within the np164_1 protein sequence, centered around amino acids 4, 114, 165, 229, 293, 322, 360, 386, 436, and 465 of SEQ ID NO:14, respectively.

np164_1 protein was expressed in a COS cell expression system, and an expressed
15 protein band of approximately 43 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "pe204_1"

A polynucleotide of the present invention has been identified as clone "pe204_1".
20 pe204_1 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe204_1 is a full-length clone, including the entire coding sequence of a secreted
25 protein (also referred to herein as "pe204_1 protein").

The nucleotide sequence of pe204_1 as presently determined is reported in SEQ ID NO:15, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe204_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:16. Amino
30 acids 116 to 128 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 129. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

the predicted leader/signal sequence not be separated from the remainder of the pe204_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe204_1 should be approximately 1100 bp.

5 The nucleotide sequence disclosed herein for pe204_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pe204_1 demonstrated at least some similarity with sequences identified as AA279961 (zs92h08.s1 NCI_CGAP_GCB1 Homo sapiens cDNA clone 704991 3'), AA306911 (EST178043 Colon carcinoma (HCC) cell line Homo sapiens cDNA 5' end),
10 AC002086 (Human PAC clone DJ525N14), AC002094 (Genomic sequence from Human 17, complete sequence), T97749 (ye58c04.s1 Homo sapiens cDNA clone), Z74696 (Human DNA sequence from cosmid 203C2, between markers DXS6791 and DXS8038 on chromosome X contains ESTs), Z80901 (Human DNA sequence from cosmid N119A7 on chromosome 22q12-qter), and Z82245 (Human DNA sequence *** SEQUENCING IN
15 PROGRESS *** from clone 799F10; HTGS phase 1). The predicted amino acid sequence disclosed herein for pe204_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted pe204_1 protein demonstrated at least some similarity to sequences identified as K02113 (Gallus gallus vitellogenin [Gallus gallus]). Based upon sequence similarity, pe204_1 proteins and each
20 similar protein or peptide may share at least some activity. The TopPredII computer program predicts two additional potential transmembrane domains within the pe204_1 protein sequence, one centered around amino acid 50 and another around amino acid 90 of SEQ ID NO:16.

pe204_1 protein was expressed in a COS cell expression system, and an expressed
25 protein band of approximately 14 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "ya1_1"

A polynucleotide of the present invention has been identified as clone "ya1_1":
30 ya1_1 was isolated from a human adult testes cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ya1_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ya1_1 protein").

The nucleotide sequence of ya1_1 as presently determined is reported in SEQ ID NO:17, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ya1_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:18. Amino acids 330 to 342 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 343. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ya1_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ya1_1 should be approximately 1400 bp.

The nucleotide sequence disclosed herein for ya1_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ya1_1 demonstrated at least some similarity with sequences identified as AA431507 (zw76e05.r1 Soares testis NHT Homo sapiens cDNA clone 782144 5') and F03332 (H. sapiens partial cDNA sequence; clone c-1tg07). Based upon sequence similarity, ya1_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within the ya1_1 protein sequence centered around amino acid 156 and around amino acid 332 of SEQ ID NO:18, respectively. The nucleotide sequence of ya1_1 indicates that it may contain an Alu repetitive element.

ya1_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 38 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "yb8_1"

A polynucleotide of the present invention has been identified as clone "yb8_1". yb8_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb8_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb8_1 protein").

The nucleotide sequence of yb8_1 as presently determined is reported in SEQ ID NO:19, and includes a poly(A) tail. What applicants presently believe to be the proper

reading frame and the predicted amino acid sequence of the yb8_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:20. Amino acids 69 to 81 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 82. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb8_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb8_1 should be approximately 1800 bp.

10 The nucleotide sequence disclosed herein for yb8_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb8_1 demonstrated at least some similarity with sequences identified as AA418057 (zv97a06.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 767698 5' similar to TR:G1143719 G1143719 RS-REX-B), L10334 (Homo sapiens neuroendocrine-specific protein B (NSP) mRNA, complete cds), U17603 (Rattus norvegicus rS-Rex-s mRNA, complete cds), and W19986 (zb38e09.r1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 305896 5', mRNA sequence). The predicted amino acid sequence disclosed herein for yb8_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted yb8_1 protein demonstrated at least some similarity to sequences identified as L10334 (neuroendocrine-specific proteins B and C [Homo sapiens]) and U17603 (rS-Rex-s [Rattus norvegicus]). Based upon sequence similarity, yb8_1 proteins and each similar protein or peptide may share at least some activity. The predicted yb8_1 protein shows significant (60% identity) amino acid similarity to the neuro-endocrine specific protein (NSP) family of proteins. Roebroek *et al.* (1993, *J. Biol Chem.* 268: 13439, which is incorporated by reference herein) report observing three transcripts from this gene family: NSP-A (3.4 kb), -B (2.3 kb), and -C (1.8 kb); they encode proteins of 776, 356, and 208 amino acids, respectively. Roebroek *et al.* also observe that these three transcripts are identical at the 3' end and only differ over a short portion near their 5' ends, and are thus possible splice variants. NSP-A and NSP-C were found in neural and endocrine tissues while NSP-B was found only in a lung carcinoma cell line (Roebrek *et al.* state that NSP-B is "aberrant" suggesting that it might be an artifact). The C-terminal portions of the protein sequences from all three transcripts are identical. The predicted yb8_1 protein shows

strong amino acid similarity within this region and is about as long as NSP-C. Thus the predicted yb8_1 protein appears to be related to NSP-C. The TopPredII computer program predicts two potential transmembrane domains within the yb8_1 protein sequence, centered around amino acids 82 and 174 of SEQ ID NO:20, respectively.

5 yb8_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 25 kDa was detected in membrane fractions and in conditioned medium using SDS polyacrylamide gel electrophoresis.

Clone "am856_3"

10 A polynucleotide of the present invention has been identified as clone "am856_3". am856_3 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. am856_3 is a full-length
15 clone, including the entire coding sequence of a secreted protein (also referred to herein as "am856_3 protein").

The nucleotide sequence of am856_3 as presently determined is reported in SEQ ID NO:21, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the am856_3 protein
20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:22. Amino acids 23 to 35 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 36. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the am856_3
25 protein. The amino acid sequence of another protein that could be encoded by basepairs 214 to 369 of SEQ ID NO:21 is reported in SEQ ID NO:274.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone am856_3 should be approximately 2100 bp.

The nucleotide sequence disclosed herein for am856_3 was searched against the
30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. am856_3 demonstrated at least some similarity with sequences identified as M26434 (Human hypoxanthine phosphoribosyltransferase (HPRT) gene, complete cds), N71723 (yw52b09.r1 Homo sapiens cDNA clone 255833 5' similar to

gb | M87920 | HUMALNE652 Human carcinoma cell-derived Alu RNA transcript, (rRNA);
gb X77738_rna1 BAND 3 ANION TRANSPORT PROTEIN), U41196 (Human (TTTC)5
short tandem repeat polymorphism UM69, D17S1339), and X89398 (H.sapiens ung gene
for uracil DNA-glycosylase). Based upon sequence similarity, am856_3 proteins and each
5 similar protein or peptide may share at least some activity. The TopPredII computer
program predicts the amino-terminal half of the am856_3 protein sequence to be highly
hydrophobic. The nucleotide sequence of am856_3 indicates that it may contain one or
more of the following types of repetitive elements: AT-like, (TTTC)5 short tandem repeat
polymorphism UM69.

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Clone "am996_12"

A polynucleotide of the present invention has been identified as clone "am996_12".
am996_12 was isolated from a human fetal kidney cDNA library using methods which
are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was
15 identified as encoding a secreted or transmembrane protein on the basis of computer
analysis of the amino acid sequence of the encoded protein. am996_12 is a full-length
clone, including the entire coding sequence of a secreted protein (also referred to herein
as "am996_12 protein").

The nucleotide sequence of am996_12 as presently determined is reported in SEQ
20 ID NO:23, and includes a poly(A) tail. What applicants presently believe to be the proper
reading frame and the predicted amino acid sequence of the am996_12 protein
corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:24. Amino
acids 14 to 26 are a predicted leader/signal sequence, with the predicted mature amino
acid sequence beginning at amino acid 27. Due to the hydrophobic nature of the
25 predicted leader/signal sequence, it is likely to act as a transmembrane domain should
the predicted leader/signal sequence not be separated from the remainder of the
am996_12 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing
clone am996_12 should be approximately 1000 bp.

30 The nucleotide sequence disclosed herein for am996_12 was searched against the
GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
FASTA search protocols. No hits were found in the database. The TopPredII computer

program predicts two potential transmembrane domains within the am996_12 protein sequence, centered around amino acids 18 and 62 of SEQ ID NO:24, respectively.

Clone "cc69_1"

5 A polynucleotide of the present invention has been identified as clone "cc69_1". cc69_1 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cc69_1 is a full-length clone,
10 including the entire coding sequence of a secreted protein (also referred to herein as "cc69_1 protein").

The nucleotide sequence of cc69_1 as presently determined is reported in SEQ ID NO:25, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cc69_1 protein corresponding
15 to the foregoing nucleotide sequence is reported in SEQ ID NO:26.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cc69_1 should be approximately 550 bp.

The nucleotide sequence disclosed herein for cc69_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
20 FASTA search protocols. cc69_1 demonstrated at least some similarity with sequences identified as AA280712 (zs98h11.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:711717 5'), AA421250 (zu27b03.s1 Soares ovary tumor NbHOT Homo sapiens cDNA clone 739181 3'), H28886 (yp03e09.s1 Homo sapiens cDNA clone 186376 3'), and H84171 (yv87c11.r1 Homo sapiens cDNA). Based upon sequence similarity, cc69_1
25 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the cc69_1 protein sequence centered around amino acid 15 of SEQ ID NO:26.

Clone "cc162_1"

30 A polynucleotide of the present invention has been identified as clone "cc162_1". cc162_1 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer

analysis of the amino acid sequence of the encoded protein. cc162_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cc162_1 protein").

The nucleotide sequence of cc162_1 as presently determined is reported in SEQ ID NO:27, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cc162_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:28. Amino acids 2 to 14 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 15. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cc162_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cc162_1 should be approximately 785 bp.

The nucleotide sequence disclosed herein for cc162_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cc162_1 demonstrated at least some similarity with sequences identified as AA369067 (EST80419 Placenta II Homo sapiens cDNA 5' end similar to EST containing Alu repeat), L05367 (Human oligodendrocyte myelin glycoprotein (OMG) exons), and R97898 (yq60b11.r1 Homo sapiens cDNA clone 200157 5'). Based upon sequence similarity, cc162_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of cc162_1 indicates that it may contain one or more of the following types of repetitive elements: ALU, L1.

Clone "if87_1"

A polynucleotide of the present invention has been identified as clone "if87_1". if87_1 was isolated from a human adult uterus cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. if87_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "if87_1 protein").

The nucleotide sequence of if87_1 as presently determined is reported in SEQ ID NO:29, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the if87_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:30. Amino acids 8 to 20 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 21. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the if87_1 protein.

10. The EcoRI/NotI restriction fragment obtainable from the deposit containing clone if87_1 should be approximately 900 bp.

The nucleotide sequence disclosed herein for if87_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. if87_1 demonstrated at least some similarity with sequences identified as AA172949 (ms20b07.r1 Stratagene mouse skin (#937313) *Mus musculus* cDNA clone 607477 5'), AC002310 (*Homo sapiens* Chromosome 16 BAC clone CIT987-SKA-635H12 ~complete genomic sequence, complete sequence), AC003012 (Human PAC clone DJ0169K13, complete sequence), D59442 (Human fetal brain cDNA 3'-end GEN-037G12), R72810 (yl09f12.r1 *Homo sapiens* cDNA clone 157775 5' similar to contains MSR1 repetitive element), and X74358 (*P. carnea* Pod-EPPT mRNA). The predicted amino acid sequence disclosed herein for if87_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted if87_1 protein demonstrated at least some similarity to sequences identified as Z46970 (secreted acid phosphatase 2 (SAP2) [*Leishmania mexicana*]). Based upon sequence similarity, if87_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the if87_1 protein sequence centered around amino acid 58 of SEQ ID NO:30. The nucleotide sequence of if87_1 indicates that it may contain one or more of the following repetitive elements: ALU, LIMA.

30 if87_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 35 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "nn103_4"

A polynucleotide of the present invention has been identified as clone "nn103_4". nn103_4 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nn103_4 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nn103_4 protein").

The nucleotide sequence of nn103_4 as presently determined is reported in SEQ ID NO:31, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nn103_4 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:32. Amino acids 19 to 31 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 32. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nn103_4 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nn103_4 should be approximately 3500 bp.

The nucleotide sequence disclosed herein for nn103_4 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nn103_4 demonstrated at least some similarity with sequences identified as AA134609 (zn90e04.r1 Stratagene lung carcinoma 937218 Homo sapiens cDNA clone 565470 5'), AA584818 (no09e05.s1 NCI_CGAP_Phe1 Homo sapiens cDNA clone IMAGE 1100192 similar to contains L1.t1 L1 repetitive element), AC002416 (**SEQUENCING IN PROGRESS** Human Chromosome X; HTGS phase 1, 3 unordered pieces), AC002456 (Human BAC clone RG013L03 from 7q21, complete sequence), D25252 (Human randomly sequenced mRNA), Q05615 (Insert from pARC 1153), U95743 (Homo sapiens chromosome 16 BAC clone CIT987-SK65D3, complete sequence), Z22970 (H.sapiens mRNA for M130 antigen cytoplasmic variant 2), Z71182 (Human DNA sequence from pac 248J6, between markers DXS366 and DXS87 on chromosome X contains STS), Z81310 (Human DNA sequence from cosmid O19A on chromosome 6 Contains HLA DNA gene and STS), Z82253 (Human DNA sequence ** SEQUENCING

IN PROGRESS *** from clone U151E3; HTGS phase 1), and Z92547 (Human DNA sequence from PAC 863K). The predicted amino acid sequence disclosed herein for nn103_4 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nn103_4 protein demonstrated at least some similarity to sequences identified as X52235 (ORFII [Homo sapiens]). Based upon sequence similarity, nn103_4 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the nn103_4 protein sequence centered around amino acid 52 of SEQ ID NO:32. The nucleotide sequence of nn103_4 indicates that it may contain one or more of the following types of repetitive elements: L1, A, MER31.

Clone "np206_8"

A polynucleotide of the present invention has been identified as clone "np206_8". np206_8 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. np206_8 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "np206_8 protein").

The nucleotide sequence of np206_8 as presently determined is reported in SEQ ID NO:33, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the np206_8 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:34.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone np206_8 should be approximately 1900 bp.

The nucleotide sequence disclosed herein for np206_8 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. np206_8 demonstrated at least some similarity with sequences identified as AA126810 (zn87a12.r1 Stratagene lung cDNA), AC000053 (*** SEQUENCING IN PROGRESS *** Human Cosmid Clone 81a12 and 70g8; HTGS phase 2), AC002094 (Genomic sequence from Human 17, complete sequence), AC002431 (Human BAC clone RG180F08 from 7q31, complete sequence), F09069 (H. sapiens partial cDNA sequence; clone c-2we10), G33587 (human STS SHGC-50493), R37071 (yf66a08.s1

Homo sapiens cDNA clone 27020.3', U91321 (Human chromosome 16p13 BAC clone), Z68746 (Human DNA sequence from cosmid Q27, chromosome region 11p15.5), and Z92846 (Human DNA sequence from cosmid U105G4, between markers DXS366 and DXS87 on chromosome X contains ESTs). Based upon sequence similarity, np206_8 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of np206_8 indicates that it may contain one or more of the following types of repetitive elements: Alu/SVA.

Clone "nt746_4"

10 A polynucleotide of the present invention has been identified as clone "nt746_4". nt746_4 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nt746_4 is a full-
15 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nt746_4 protein").

The nucleotide sequence of nt746_4 as presently determined is reported in SEQ ID NO:35, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nt746_4 protein
20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:36.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nt746_4 should be approximately 1200 bp.

The nucleotide sequence disclosed herein for nt746_4 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
25 FASTA search protocols. nt746_4 demonstrated at least some similarity with sequences identified as AA489740 (aa43c06.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 8236905'), J04989 (Bovine alpha 1-3 galactosyltransferase mRNA completed cds), M60263 (Human alpha-1,3-galactosyltransferase (HGT-2) pseudogene), Q74712 (Galactosyl transferase clone), R24770 (yg42c11.r1 Homo sapiens cDNA clone 35316 5' similar to SP
30 GATR_BOVIN P14769 N-ACETYLLACTOSAMINIDE ALPHA-1,3-GALACTOSYL-TRANSFERASE), and S71333 (alpha 1,3 galactosyltransferase [New World monkeys, mermoset lymphoid cell line B95.8, mRNA Partial, 1131 nt]). The predicted amino acid sequence disclosed herein for nt746_4 was searched against the GenPept and GeneSeq

amino acid sequence databases using the BLASTX search protocol. The predicted nt746_4 protein demonstrated at least some similarity to sequences identified as M26925 (galactosyltransferase (EC 2.4.1.151) [Mus musculus]), R80016 (Marmoset alpha-1,3-galactosyltransferase), S71333 (alpha 1,3 galactosyltransferase, alpha 1,3GT [New World monkeys, marmoset lymphoid cell line B95.8, Peptide, 376 aa] [Platyrrhini]), and W13639 (Murine alpha(1,3)-galactosyltransferase). Based upon sequence similarity, nt746_4 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the nt746_4 protein sequence centered around amino acid 15 of SEQ ID NO:36. The nucleotide sequence of nt746_4 indicates that it may contain an LTR repetitive element.

nt746_4 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 100 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

15 Clone "pe286_1"

A polynucleotide of the present invention has been identified as clone "pe286_1". pe286_1 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe286_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pe286_1 protein").

The nucleotide sequence of pe286_1 as presently determined is reported in SEQ ID NO:37, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe286_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:38.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe286_1 should be approximately 300 bp.

The nucleotide sequence disclosed herein for pe286_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pe286_1 demonstrated at least some similarity with sequences identified as AA588854 (no21h03.s1 NCI_CGAP_Pr22 Homo sapiens cDNA clone IMAGE 1101365), L46897 (Homo sapiens (subclone 3_d9 from P1 H13) DNA sequence), and

N48057 (yy99d09.s1 Homo sapiens cDNA clone 281681 3' similar to contains element MER4 repetitive element). Based upon sequence similarity, pe286_1 proteins and each similar protein or peptide may share at least some activity.

5 Clone "yb7_1"

A polynucleotide of the present invention has been identified as clone "yb7_1". yb7_1 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer
10 analysis of the amino acid sequence of the encoded protein. yb7_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb7_1 protein").

The nucleotide sequence of yb7_1 as presently determined is reported in SEQ ID NO:39, and includes a poly(A) tail. What applicants presently believe to be the proper
15 reading frame and the predicted amino acid sequence of the yb7_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:40.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb7_1 should be approximately 1150 bp.

The nucleotide sequence disclosed herein for yb7_1 was searched against the
20 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb7_1 demonstrated at least some similarity with sequences identified as N99344 (IMAGE:20090 Homo sapiens cDNA clone 20090). Based upon sequence similarity, yb7_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane
25 domain within the yb7_1 protein sequence located around amino acid 52 of SEQ ID NO:40; this domain is also a potential leader/signal sequence with the mature protein beginning at or near amino acid 52 of SEQ ID NO:40.

Clone "am728_60"

30 A polynucleotide of the present invention has been identified as clone "am728_60". am728_60 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis

of computer analysis of the amino acid sequence of the encoded protein. am728_60 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "am728_60 protein").

The nucleotide sequence of am728_60 as presently determined is reported in SEQ ID NO:41. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the am728_60 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:42.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone am728_60 should be approximately 4333 bp.

10 The nucleotide sequence disclosed herein for am728_60 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. am728_60 demonstrated at least some similarity with sequences identified as AA446039 (zw66a08.r1 Soares testis NHT Homo sapiens cDNA clone 781142 5') and U73682 (Human meningioma-expressed antigen 11 (MEA11) mRNA, partial cds).
15 The predicted amino acid sequence disclosed herein for am728_60 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted am728_60 protein demonstrated at least some similarity to sequences identified as U67884 (melanoma inhibitory activity/condrocyte-derived retinoic acid sensitive protein homolog [Rattus norvegicus]), U73682
20 (meningioma-expressed antigen 11 [Homo sapiens]), U94780 (MEA6 [Homo sapiens]), and X84707 (melanoma growth regulatory protein [Homo sapiens]). Based upon sequence similarity, am728_60 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three potential transmembrane domains within the am728_60 protein sequence, centered around amino
25 acids 300, 370, and 670 of SEQ ID NO:42, respectively.

When expressed in COS cells, am728_60 protein was detected in a membrane fraction from these cells as a band migrating at approximately 200 kD on a denaturing SDS polyacrylamide gel.

30 Clone "bf377_1"

A polynucleotide of the present invention has been identified as clone "bf377_1". bf377_1 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was

identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bf377_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bf377_1 protein").

5 The nucleotide sequence of bf377_1 as presently determined is reported in SEQ ID NO:43, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bf377_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:44. Amino acids 27 to 39 of SEQ ID NO:44 are a predicted leader/signal sequence, with the predicted
10 mature amino acid sequence beginning at amino acid 40. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bf377_1 protein.

 The EcoRI/NotI restriction fragment obtainable from the deposit containing
15 clone bf377_1 should be approximately 450 bp.

 The nucleotide sequence disclosed herein for bf377_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bf377_1 demonstrated at least some similarity with sequences identified as AA559859 (nl48c05.s1 NCI_CGAP_Pr4 Homo sapiens cDNA clone IMAGE
20 1043912), AA657838 (nu08b11.s1 NCI_CGAP_Pr2 Homo sapiens cDNA clone IMAGE:1207389 similar to gb:M15990 PROTO-ONCOGENE TYROSINE-PROTEIN KINASE YES (HUMAN)), and R49353 (yg67e07.s1 Homo sapiens cDNA clone 38126 3' similar to contains MER22 repetitive element). Based upon sequence similarity, bf377_1 proteins and each similar protein or peptide may share at least some activity.

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Clone "cw354_1"

 A polynucleotide of the present invention has been identified as clone "cw354_1". cw354_1 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was
30 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cw354_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cw354_1 protein").

The nucleotide sequence of cw354_1 as presently determined is reported in SEQ ID NO:45, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cw354_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:46. Amino acids 28 to 40 of SEQ ID NO:46 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 41. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cw354_1 protein.

10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cw354_1 should be approximately 1350 bp.

The nucleotide sequence disclosed herein for cw354_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cw354_1 demonstrated at least some similarity with sequences identified as D58859 (Human placenta cDNA 5'-end GEN-514B03), H07863 (yl86b05.s1 Homo sapiens cDNA clone 45017 3'), N32178 (yy25b09.s1 Homo sapiens cDNA clone 272249 3'), R81953 (yi98e11.r1 Homo sapiens cDNA clone 147308 5'), and W84437 (zd89d06.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 356651 3'). The predicted amino acid sequence disclosed herein for cw354_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted cw354_1 protein demonstrated at least some similarity to sequences identified as U39726 (adenosinetriphosphatase [Mycoplasma genitalium]). Based upon sequence similarity, cw354_1 proteins and each similar protein or peptide may share at least some activity.

25

Clone "nm134_4"

A polynucleotide of the present invention has been identified as clone "nm134_4". nm134_4 was isolated from a human adult blood (erythroleukemia TF-1) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nm134_4 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nm134_4 protein").

The nucleotide sequence of nm134_4 as presently determined is reported in SEQ ID NO:47, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nm134_4 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:48. Amino acids 136 to 148 of SEQ ID NO:48 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 149. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nm134_4 protein.

10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nm134_4 should be approximately 1500 bp.

The nucleotide sequence disclosed herein for nm134_4 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nm134_4 demonstrated at least some similarity with sequences identified as AA205020 (zq72a12.r1 Stratagene neuroepithelium (#937231) Homo sapiens cDNA clone 647134 5'), AA205286 (zq72a12.s1 Stratagene neuroepithelium (#937231) Homo sapiens cDNA clone 647134 3'), AA261864 (zs18h05.r1 Soares NbHTGBC Homo sapiens cDNA clone 685593 5'), and H63680 (yr55d03.r1 Homo sapiens cDNA clone 209189 5'). Based upon sequence similarity, nm134_4 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts five potential transmembrane domains within the nm134_4 protein sequence centered around amino acids 108, 132, 170, 195, and 226 of SEQ ID NO:48, respectively.

Clone "yb11_1"

25 A polynucleotide of the present invention has been identified as clone "yb11_1". yb11_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb11_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb11_1 protein").

30 The nucleotide sequence of yb11_1 as presently determined is reported in SEQ ID NO:49, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb11_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:50. Amino

acids 43 to 55 of SEQ ID NO:50 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 56. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb11_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb11_1 should be approximately 2800 bp.

The nucleotide sequence disclosed herein for yb11_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb11_1 demonstrated at least some similarity with sequences identified as R55695 (yg88f12.s1 Homo sapiens cDNA clone 40397.3') and R85100 (yo43b05.s1 Homo sapiens cDNA clone 180657.3'). Based upon sequence similarity, yb11_1 proteins and each similar protein or peptide may share at least some activity.

Clone "yc2_1"

A polynucleotide of the present invention has been identified as clone "yc2_1". yc2_1 was isolated from a human fetal kidney (293 cell line) cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yc2_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yc2_1 protein").

The nucleotide sequence of yc2_1 as presently determined is reported in SEQ ID NO:51, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yc2_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:52. Amino acids 15 to 27 of SEQ ID NO:52 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 28. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yc2_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yc2_1 should be approximately 2900 bp.

The nucleotide sequence disclosed herein for yc2_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yc2_1 demonstrated at least some similarity with sequences identified as AA618531 (np38a03.s1 NCL_CGAP_Lu1 Homo sapiens cDNA clone IMAGE:1118572 similar to contains Alu repetitive element) and AA626937 (af84h07.s1 Soares testis NHT Homo sapiens cDNA clone 1048765 3'). Based upon sequence similarity, yc2_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of yc2_1 indicates that it may contain one or more Alu repetitive elements.

10

Clone "ff168_12"

A polynucleotide of the present invention has been identified as clone "ff168_12". ff168_12 was isolated from a human adult testes (teratocarcinoma NCCTT) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ff168_12 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ff168_12 protein").

The nucleotide sequence of ff168_12 as presently determined is reported in SEQ ID NO:53, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ff168_12 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:54.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ff168_12 should be approximately 1600 bp.

The nucleotide sequence disclosed herein for ff168_12 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ff168_12 demonstrated at least some similarity with sequences identified as AA025945 (ze91e02.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 366362 5'), AA156237 (zl50c09.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 505360 3'), AA420993 (zu08e09.s1 Soares testis NHT Homo sapiens cDNA clone 731272 3'), N78486 (yz78e03.r1 Homo sapiens cDNA clone 289180 5'), W01843 (za80a01.r1 Soares fetal lung NbHL19W Homo sapiens cDNA clone 298824 5'), and W95777 (ze07e02.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 358298 5').

Based upon sequence similarity, ff168_12 proteins and each similar protein or peptide may share at least some activity.

Clone "ls9_1"

5 A polynucleotide of the present invention has been identified as clone "ls9_1". ls9_1 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ls9_1 is a full-
10 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ls9_1 protein").

The nucleotide sequence of ls9_1 as presently determined is reported in SEQ ID NO:55, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ls9_1 protein corresponding
15 to the foregoing nucleotide sequence is reported in SEQ ID NO:56. Amino acids 60 to 72 of SEQ ID NO:56 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 73. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ls9_1
20 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ls9_1 should be approximately 2300 bp.

The nucleotide sequence disclosed herein for ls9_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
25 FASTA search protocols. ls9_1 demonstrated at least some similarity with sequences identified as AA527586 (ng42d05.s1 NCI_CGAP_Co3 Homo sapiens cDNA clone IMAGE:937449), AC000119 (Human BAC clone RG104I04 from 7q21-7q22, complete sequence), T18551 (Human polycystic kidney disease normal PKD1 gene), Y10196 (H.sapiens PEX gene), and Z94721 (Human DNA sequence *** SEQUENCING IN
30 PROGRESS *** from clone 167A14; HTGS phase 1). The predicted amino acid sequence disclosed herein for ls9_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted ls9_1 protein demonstrated at least some similarity to sequences identified as AB002375 (K1AA0377

[Homo sapiens]) and R95913 (Neural thread protein). Based upon sequence similarity, ls9_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the ls9_1 protein sequence centered around amino acid 40 of SEQ ID NO:56. The
5 nucleotide sequence of ls9_1 indicates that it may contain an Alu/SVA repetitive element.

Clone "na1010_1"

A polynucleotide of the present invention has been identified as clone "na1010_1". na1010_1 was isolated from a human adult brain cDNA library using methods which are
10 selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. na1010_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na1010_1 protein").

15 The nucleotide sequence of na1010_1 as presently determined is reported in SEQ ID NO:57, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the na1010_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:58. Amino acids 24 to 36 of SEQ ID NO:58 are a predicted leader/signal sequence, with the predicted
20 mature amino acid sequence beginning at amino acid 37. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na1010_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing
25 clone na1010_1 should be approximately 1050 bp.

The nucleotide sequence disclosed herein for na1010_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. na1010_1 demonstrated at least some similarity with sequences identified as AC002091 (Genomic sequence from Human 17, complete sequence),
30 AC002382 (Human BAC clone RG022J17 from 7q21, complete sequence), and M26434 (Human hypoxanthine phosphoribosyltransferase (HPRT) gene, complete cds). Based upon sequence similarity, na1010_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of na1010_1 indicates that it may

contain one or more of the following repetitive elements: L1/A/MIR/SVA/LTRII, Alu/SVA/A/GAA, or Alu/A/GAAAA.

Clone "nf87_1"

5 A polynucleotide of the present invention has been identified as clone "nf87_1". nf87_1 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nf87_1 is a full-
10 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nf87_1 protein").

The nucleotide sequence of nf87_1 as presently determined is reported in SEQ ID NO:59, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nf87_1 protein corresponding
15 to the foregoing nucleotide sequence is reported in SEQ ID NO:60. Amino acids 53 to 65 of SEQ ID NO:60 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 66. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nf87_1
20 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nf87_1 should be approximately 1200 bp.

The nucleotide sequence disclosed herein for nf87_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
25 FASTA search protocols. nf87_1 demonstrated at least some similarity with sequences identified as AA358277 (EST67398 Fetal lung III Homo sapiens cDNA 5' end similar to similar to interferon-alpha-inducible gene p27), W52706 (zc55g02.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 326258 5' similar to SW INI7_HUMAN P40305 INTERFERON-ALPHA INDUCED 11.5 KD PROTEIN), and X67325 (H.sapiens
30 p27 mRNA). The predicted amino acid sequence disclosed herein for nf87_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nf87_1 protein demonstrated at least some similarity to sequences identified as X67325 (p27 gene product [Homo sapiens]). The

interferon-alpha-inducible gene is localized on human chromosome 14q32 and expresses the highly hydrophobic p27 gene product in breast carcinoma cells. Based upon sequence similarity, nf87_1 proteins and each similar protein or peptide may share at least some activity.

5 nf87_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 16 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "nh796_1"

10 A polynucleotide of the present invention has been identified as clone "nh796_1". nh796_1 was isolated from a human adult brain (thalamus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nh796_1 is a full-
15 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nh796_1 protein").

The nucleotide sequence of nh796_1 as presently determined is reported in SEQ ID NO:61, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nh796_1 protein
20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:62. Amino acids 7 to 19 of SEQ ID NO:62 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 20. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the
25 nh796_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nh796_1 should be approximately 1050 bp.

The nucleotide sequence disclosed herein for nh796_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
30 FASTA search protocols. nh796_1 demonstrated at least some similarity with sequences identified as AA315985 (EST18772 Lung Homo sapiens cDNA 5' end), N23239 (yw47b07.s1 Homo sapiens cDNA clone 255349 3'), N27741 (yw51c06.s1 Homo sapiens cDNA clone 255754 3'), U69172 (Mus musculus unknown protein mRNA, complete cds),

and Z24371 (H. sapiens (D20S195) DNA segment containing (CA) repeat; clone AFM321xc1; single read). The predicted amino acid sequence disclosed herein for nh796_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nh796_1 protein demonstrated at least
5 some similarity to sequences identified as U69172 (unknown [Mus musculus]). The mouse protein of unknown function (U69172) is expressed in late palate development. Based upon sequence similarity, nh796_1 proteins and each similar protein or peptide may share at least some activity.

nh796_1 protein was expressed in a COS cell expression system, and an expressed
10 protein band of approximately 25 kDa was detected in conditioned media and membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "nn229_1"

A polynucleotide of the present invention has been identified as clone "nn229_1".
15 nn229_1 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nn229_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred
20 to herein as "nn229_1 protein").

The nucleotide sequence of nn229_1 as presently determined is reported in SEQ ID NO:63, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nn229_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:64. Amino
25 acids 59 to 71 of SEQ ID NO:64 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 72. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nn229_1 protein.

30 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nn229_1 should be approximately 1050 bp.

The nucleotide sequence disclosed herein for nn229_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and

FASTA search protocols. nn229_1 demonstrated at least some similarity with sequences identified as H24014 (ym49f02.s1 Homo sapiens cDNA clone 51480 3'), R08508 (ye95h01.r1 Homo sapiens cDNA clone 125521 5' similar to gb|M87910|HUMALNE34 Human carcinoma cell-derived Alu RNA transcript, (rRNA); gb|J02931|TISSUE FACTOR PRECURSOR (HUMAN)), and Z96508 (H.sapiens telomeric DNA sequence, clone 22QTEL030, read 22QTELOO030.seq). Based upon sequence similarity, nn229_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the nn229_1 protein sequence centered around amino acid 20 of SEQ ID NO:64. The nucleotide sequence of nn229_1 indicates that it may contain a MER20 repetitive element.

Clone "np156_1"

A polynucleotide of the present invention has been identified as clone "np156_1". np156_1 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. np156_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "np156_1 protein").

The nucleotide sequence of np156_1 as presently determined is reported in SEQ ID NO:65, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the np156_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:66. Amino acids 6 to 18 of SEQ ID NO:66 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 19. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the np156_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone np156_1 should be approximately 1200 bp.

The nucleotide sequence disclosed herein for np156_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. np156_1 demonstrated at least some similarity with sequences

identified as AA298580 (EST114211 HSC172 cells I Homo sapiens cDNA 5' end), AA447514 (zw81a05.s1 Soares testis NHT Homo sapiens cDNA clone 782576 3'), AC002309 (** SEQUENCING IN PROGRESS ** Human Chromosome 22q11 Cosmid Clone 63e9; HTGS phase 1, 3 unordered pieces), AF007269 (Arabidopsis thaliana BAC IG002N01), and N53641 (yz04g03.r1 Homo sapiens cDNA clone 282100 5'). Based upon sequence similarity, np156_1 proteins and each similar protein or peptide may share at least some activity.

Clone "bg570_1"

1.0 A polynucleotide of the present invention has been identified as clone "bg570_1". bg570_1 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bg570_1 is a full-length clone, 15 including the entire coding sequence of a secreted protein (also referred to herein as "bg570_1 protein").

The nucleotide sequence of bg570_1 as presently determined is reported in SEQ ID NO:67, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bg570_1 protein 20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:68. Amino acids 33 to 45 of SEQ ID NO:68 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 46. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the 25 bg570_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bg570_1 should be approximately 900 bp.

The nucleotide sequence disclosed herein for bg570_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and 30 FASTA search protocols. bg570_1 demonstrated at least some similarity with sequences identified as T03370 (IB1429 Infant brain, Bento Soares Homo sapiens cDNA clone IB1429 3'end). Based upon sequence similarity, bg570_1 proteins and each similar protein or peptide may share at least some activity.

Clone "bi120_2"

A polynucleotide of the present invention has been identified as clone "bi120_2". bi120_2 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was
5 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bi120_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bi120_2 protein").

The nucleotide sequence of bi120_2 as presently determined is reported in SEQ ID
10 NO:69, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bi120_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:70. Amino acids 39 to 51 of SEQ ID NO:70 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 52. Due to the hydrophobic nature
15 of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bi120_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bi120_2 should be approximately 1800 bp.

20 The nucleotide sequence disclosed herein for bi120_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bi120_2 demonstrated at least some similarity with sequences identified as AA232119 (zr24a12.r1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 664318 5' similar to WP:C11H1.2 CE05261), D20759 (Human HL60
25 3'directed MboI cDNA, HUMGS01738, clone mp1051), N28753 (yx67h11.r1 Homo sapiens cDNA clone), N28806 (yx70g12.r1 Homo sapiens cDNA clone 267142 5'), N35232 (yy21d02.s1 Homo sapiens cDNA clone 271875 3'), W73805 (zd50g02.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 344114 5'), Z61133 (H.sapiens CpG island DNA genomic MseI fragment, clone 45g1, forward read cpg45g1.ft1a), and Z70205
30 (Caenorhabditis elegans cosmid C11H1, complete sequence). bi120_2 also demonstrated at least some similarity with CpG island DNA. The predicted amino acid sequence disclosed herein for bi120_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted bi120_2 protein

demonstrated at least some similarity to sequences identified as Z70205 (C11H1.2 [Caenorhabditis elegans]). Based upon sequence similarity, bi120_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts five additional potential transmembrane domains within the bi120_2 protein sequence, centered around amino acids 20, 80, 110, 150, and 290 of SEQ ID NO:70, respectively. There may be a frameshift in the full-clone sequence (somewhere within base pairs 990-1010 of SEQ ID NO:69). This frameshift from reading frame 3 to reading frame 1 would extend the open reading frame from 309 amino acids to at least 460 amino acids and add three more potential transmembrane domains to the protein. There also appears to be another frameshift occurring around base pair 1450 of SEQ ID NO:69 which shifts the open reading frame back into frame 3, adding approximately 20 more codons to the open reading frame sequence.

Clone "bn594_1"

A polynucleotide of the present invention has been identified as clone "bn594_1". bn594_1 was isolated from a human adult placenta cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bn594_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bn594_1 protein").

The nucleotide sequence of bn594_1 as presently determined is reported in SEQ ID NO:71, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bn594_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:72.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bn594_1 should be approximately 1400 bp.

The nucleotide sequence disclosed herein for bn594_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bn594_1 demonstrated at least some similarity with sequences identified as J03071 (Human growth hormone (GH-1 and GH-2) and chorionic somatomammotropin (CS-1, CS-2 and CS-5) genes, complete cds). Based upon sequence similarity, bn594_1 proteins and each similar protein or peptide may share at least some

activity. The TopPredII computer program predicts a potential transmembrane domain within the bn594_1 protein sequence centered around amino acid 52 of SEQ ID NO:72; this region is also a potential signal sequence, with the mature protein starting at amino acid 53 of SEQ ID NO:72. The nucleotide sequence of bn594_1 indicates that it may
5 contain one or more of the following types of repetitive elements: ALU, GAAA.

Clone "en554_1"

A polynucleotide of the present invention has been identified as clone "en554_1". en554_1 was isolated from a human fetal brain cDNA library using methods which are
10 selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. en554_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "en554_1 protein").

15 The nucleotide sequence of en554_1 as presently determined is reported in SEQ ID NO:73, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the en554_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:74. Amino acids 15 to 27 of SEQ ID NO:74 are a predicted leader/signal sequence, with the predicted
20 mature amino acid sequence beginning at amino acid 28. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the en554_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing
25 clone en554_1 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for en554_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. en554_1 demonstrated at least some similarity with sequences identified as AA625842 (zv87d08.s1 Soares NhHMPu S1 Homo sapiens cDNA clone
30 766767 3') and R54550 (yg75h06.r1 Homo sapiens cDNA clone 39297 5'). Based upon sequence similarity, en554_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of en554_1 indicates that it may contain repetitive elements in the region between base pairs 849 and 1023 of SEQ ID NO:73.

Clone "na474_10"

A polynucleotide of the present invention has been identified as clone "na474_10". na474_10 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. na474_10 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na474_10 protein").

The nucleotide sequence of na474_10 as presently determined is reported in SEQ ID NO:75, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the na474_10 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:76. Amino acids 69 to 81 of SEQ ID NO:76 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 82. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na474_10 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na474_10 should be approximately 1500 bp.

The nucleotide sequence disclosed herein for na474_10 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. na474_10 demonstrated at least some similarity with sequences identified as AA262604 (zs23f01.s1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:686041 3' similar to contains Alu repetitive element), AA450131 (zx42a02.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 789098 5'), U72661 (Human ninjurin1 mRNA, complete cds), and W38567 (zb20h04.r1 Soares fetal lung NbHL19W Homo sapiens cDNA clone 302647 5'). The predicted amino acid sequence disclosed herein for na474_10 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted na474_10 protein demonstrated at least some similarity to sequences identified as U72661 (ninjurin1 [Homo sapiens]). Based upon sequence similarity, na474_10 proteins and each similar protein or peptide may share at least some activity. Ninjurin is a cell-surface protein and adhesion molecule which is induced by nerve injury and promotes axonal growth.

Ninjurin is capable of mediating homophilic adhesion and can promote neurite extension of dorsal root ganglion neurons *in vitro*. It is thought to play a role in nerve regeneration and in the formation and function of other tissues (Araki *et al.*, 1996, *Neuron* 17(2):353-361, incorporated herein by reference). na474_10 and ninjurin appear to define a novel family of adhesion molecules.

na474_10 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 15 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

10 Clone "nn16_10"

A polynucleotide of the present invention has been identified as clone "nn16_10". nn16_10 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nn16_10 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nn16_10 protein").

The nucleotide sequence of nn16_10 as presently determined is reported in SEQ ID NO:77, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nn16_10 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:78. Amino acids 14 to 26 of SEQ ID NO:78 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 27. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nn16_10 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nn16_10 should be approximately 1600 bp.

The nucleotide sequence disclosed herein for nn16_10 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nn16_10 demonstrated at least some similarity with sequences identified as R46973 (Y224 *Rattus norvegicus* cDNA clone Y224 5' end), U43404 (*Sus scrofa* ameloblastin mRNA, complete cds), W13000 (mb21d12.r1 Soares mouse

p3NMF19.5 *Mus musculus* cDNA clone 330071 5'), and W36463 (mb71c12.r1 Soares mouse p3NMF19.5 *Mus musculus* cDNA clone 334870 5'). The predicted amino acid sequence disclosed herein for nn16_10 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted
5 nn16_10 protein demonstrated at least some similarity to sequences identified as U43404 (ameloblastin [*Sus scrofa*]), and to the ameloblastin proteins of rat (and other species). Ameloblastin is a unique ameloblast-specific gene product that may be important in enamel matrix formation and mineralization (Krebsbach *et al.*, 1996, *J. Biol. Chem.* 271: 4431, incorporated herein by reference). Rat ameloblastin is 442 amino acids and is a
10 tooth-specific enamel matrix protein. Immunohistochemical data show staining of golgi and of secretory granules of the secretory ameloblast, in addition to the entire thickness of the enamel matrix. The rat ameloblastin protein is synthesized as a 55 kDa core protein which undergoes extensive post-translational modifications with O-linked oligo-
15 *Cytochem.* 45(10):1329-1340, incorporated herein by reference). Based upon sequence similarity, nn16_10 proteins and each similar protein or peptide may share at least some activity.

nn16_10 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 84 kDa was detected in conditioned medium and
20 membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "np189_9"

A polynucleotide of the present invention has been identified as clone "np189_9". np189_9 was isolated from a human fetal kidney (293 cell line) cDNA library using
25 methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. np189_9 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "np189_9 protein").

30 The nucleotide sequence of np189_9 as presently determined is reported in SEQ ID NO:79, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the np189_9 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:80. Amino

acids 41 to 53 of SEQ ID NO:80 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 54. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the np189_9 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone np189_9 should be approximately 2100 bp.

The nucleotide sequence disclosed herein for np189_9 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. np189_9 demonstrated at least some similarity with sequences identified as AA035196 (zk27f12.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 471791 3'), AA336568 (EST41447 Endometrial tumor Homo sapiens cDNA 5' end), AA420972 (zt86a11.s1 Soares testis NHT Homo sapiens cDNA clone 729212 3'), and H38460 (yp69h08.s1 Homo sapiens cDNA clone 192735 3'). Based upon sequence similarity, np189_9 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the np189_9 protein sequence centered around amino acid 38 of SEQ ID NO:80.

Clone "ny226_1"

A polynucleotide of the present invention has been identified as clone "ny226_1". ny226_1 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ny226_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ny226_1 protein").

The nucleotide sequence of ny226_1 as presently determined is reported in SEQ ID NO:81, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ny226_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:82.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ny226_1 should be approximately 3175 bp.

The nucleotide sequence disclosed herein for ny226_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ny226_1 demonstrated at least some similarity with sequences identified as AC002463 (Human BAC clone RG302F04 from 7q31, complete sequence),
5 R07637 (ye98e03.s1 Homo sapiens cDNA clone 125788 3'), and Z78730 (H.sapiens flow-sorted chromosome 6 HindIII fragment, SC6pA15C3). Based upon sequence similarity, ny226_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the ny226_1 protein sequence centered around amino acid 22 of SEQ ID NO:82;
10 this region is also a putative signal sequence, with the mature protein starting at amino acid 23 of SEQ ID NO:82. The nucleotide sequence of ny226_1 indicates that it may contain one or more repetitive elements, including ALU repetitive elements.

Clone "pe159_1"

15 A polynucleotide of the present invention has been identified as clone "pe159_1". pe159_1 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded
20 protein. pe159_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pe159_1 protein").

The nucleotide sequence of pe159_1 as presently determined is reported in SEQ ID NO:83, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe159_1 protein
25 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:84.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe159_1 should be approximately 1000 bp.

The nucleotide sequence disclosed herein for pe159_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
30 FASTA search protocols. pe159_1 demonstrated at least some similarity with sequences identified as AA372974 (EST84925 Colon adenocarcinoma IV Homo sapiens cDNA 5' end), AC002377 (Human PAC clone Dj222H05), AC002519 (** SEQUENCING IN PROGRESS ** Human chromosome 16p11.2 BAC clone CIT987SK-A-355G7; HTGS phase

2, 1 ordered pieces), H45355 (yn99b01.r1 Homo sapiens cDNA clone 176521 5'), W39648 (zc19c09.r1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 322768 5'), and Z84816 (Human DNA sequence from PAC 2A2 on chromosome X contains ESTs). The predicted amino acid sequence disclosed herein for pe159_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted pe159_1 protein demonstrated at least some similarity to sequences identified as M84237 (integrin beta-1 subunit [Homo sapiens]) and R96800 (Human histiocyte-secreted factor HSF). Based upon sequence similarity, pe159_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of pe159_1 indicates that it may contain one or more of the following types of repetitive elements: Alu, SVA, MER3.

Clone "pj314_8"

A polynucleotide of the present invention has been identified as clone "pj314_8". pj314_8 was isolated from a human fetal carcinoma (cell type NTD2 treated with retinoic acid for 23 days) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pj314_8 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pj314_8 protein").

The nucleotide sequence of pj314_8 as presently determined is reported in SEQ ID NO:85, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pj314_8 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:86. Amino acids 23 to 35 of SEQ ID NO:86 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 36. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pj314_8 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pj314_8 should be approximately 1200 bp.

The nucleotide sequence disclosed herein for pj314_8 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and

FASTA search protocols. pj314_8 demonstrated at least some similarity with sequences identified as H98510 (yv90g02.r1 Homo sapiens cDNA clone), U03019 (Human melanoma growth stimulatory activity beta (MGSA beta) gene, partial cds), U25660 (Dictyostelium discoideum actin gene, partial cds), W67504 (zd40f09.s1 Soares fetal heart NbHH19W
5 Homo sapiens cDNA clone 343145 3'), Z99358 (Homo sapiens mRNA; expressed sequence tag; clone DKFZphamy1_1a3, 5' read), and Z99359 (Homo sapiens mRNA; expressed sequence tag; clone DKFZphamy1_1a3, 3' read). The predicted amino acid sequence disclosed herein for pj314_8 was searched against the GenPept and GeneSeq amino acid
10 demonstrated at least some similarity to sequences identified as U16359 (nitric oxide synthase [Rattus norvegicus]). Based upon sequence similarity, pj314_8 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of pj314_8 indicates that it may contain one or more of the following types of repetitive elements: AC repeats, PAB repeats, CA repeats.

15

Clone "bp870_1"

A polynucleotide of the present invention has been identified as clone "bp870_1". bp870_1 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was
20 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bp870_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bp870_1 protein").

The nucleotide sequence of bp870_1 as presently determined is reported in SEQ
25 ID NO:87, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bp870_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:88. Amino acids 9 to 21 of SEQ ID NO:88 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 22. Due to the hydrophobic nature
30 of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bp870_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bp870_1 should be approximately 1000 bp.

The nucleotide sequence disclosed herein for bp870_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bp870_1 demonstrated at least some similarity with sequences identified as AA229935 (nc51g10.r1 NCI_CGAP_Pr3 Homo sapiens cDNA clone IMAGE:1011714 similar to contains Alu repetitive element; contains element MER4 repetitive element), H12643 (yj13a04.r1 Homo sapiens cDNA clone 1485905'), and H12594 (yj13a04.s1 Homo sapiens cDNA clone 148590 3' similar to contains Alu repetitive element). Based upon sequence similarity, bp870_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of bp870_1 indicates that it may contain a simple repeat region and at least one copy of an Alu repetitive element.

bp870_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 23 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "bx141_2"

A polynucleotide of the present invention has been identified as clone "bx141_2". bx141_2 was isolated from a human adult ovary (PA-1 teratocarcinoma, pool of retinoic-acid-treated, activin-treated, and untreated tissue) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bx141_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bx141_2 protein").

The nucleotide sequence of bx141_2 as presently determined is reported in SEQ ID NO:89, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bx141_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:90. Amino acids 30 to 42 of SEQ ID NO:90 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 43. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain

should the predicted leader/signal sequence not be separated from the remainder of the bx141_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bx141_2 should be approximately 1800 bp.

- 5 The nucleotide sequence disclosed herein for bx141_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bx141_2 demonstrated at least some similarity with sequences identified as AA173353 (zp32b01.r1 Stratagene neuroepithelium (#937231) Homo sapiens cDNA clone 611113 5' similar to SW:A15_HUMAN P41732 CELL SURFACE
- 10 GLYCOPROTEIN A15), AA375927 (EST88303 HSC172 cells II Homo sapiens cDNA 5' end similar to similar to cell surface glycoprotein), D10653 (Human mRNA for cell surface glycoprotein, complete cds), H64050 (yr58c07.r1 Homo sapiens cDNA clone 209484 5' similar to SP:S39262 S39262 PLATELET CELL SURFACE GLYCOPROTEIN), and R41866 (yg12f04.s1 Homo sapiens cDNA clone 31854 3'). The predicted amino acid sequence
- 15 disclosed herein for bx141_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted bx141_2 protein demonstrated at least some similarity to sequences identified as D10653 (HUMA15_1 cell surface glycoprotein [Homo sapiens]) and D29808 (HUMTALLA1_1 TALLA-1 [Homo sapiens]). The human cell surface glycoprotein ("D10653 protein") is a protein of 244
- 20 amino acids which contains four potential transmembrane domains and four possible N-linked glycosylation sites. A computer-aided comparison showed a marked similarity between D10653 protein and several other membrane proteins: CD9, CD37, CD53, TAPA-1, Sm23, CO-029, and ME491/CD63; also, D10653 protein is similar to the ME491/CD63 protein superfamily. bx141_2 protein also shows some similarity to the
- 25 human and mouse ME491 and CD63 proteins. Based upon sequence similarity, bx141_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four potential transmembrane domains within the bx141_2 protein sequence centered around amino acids 31, 70, 104, and 222 of SEQ ID NO:90, respectively.
- 30 bx141_2 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 24 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "cw272_7"

A polynucleotide of the present invention has been identified as clone "cw272_7". cw272_7 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was
5 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cw272_7 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cw272_7 protein").

The nucleotide sequence of cw272_7 as presently determined is reported in SEQ
10 ID NO:91, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cw272_7 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:92. Amino acids 48 to 60 of SEQ ID NO:92 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 61. Due to the hydrophobic nature
15 of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cw272_7 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cw272_7 should be approximately 2300 bp.

20 The nucleotide sequence disclosed herein for cw272_7 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. While no clear hits were found in these databases, cw272_7 protein does show some similarity to bone morphogenetic proteins and procollagens.

Clone "nh328_5"

25 A polynucleotide of the present invention has been identified as clone "nh328_5". nh328_5 was isolated from a human adult brain (thalamus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of
30 computer analysis of the amino acid sequence of the encoded protein. nh328_5 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nh328_5 protein").

The nucleotide sequence of nh328_5 as presently determined is reported in SEQ ID NO:93, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nh328_5 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:94. Amino acids 60 to 72 of SEQ ID NO:94 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 73. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nh328_5 protein.

10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nh328_5 should be approximately 2200 bp.

The nucleotide sequence disclosed herein for nh328_5 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nh328_5 demonstrated at least some similarity with sequences identified as AA426157 (zv83a09.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 760216 5'), D17160 (Human HepG2 3' region MboI cDNA, clone hmd2d01m3), D56329 (Human fetal brain cDNA 5'-end GEN-424F08), N62903 (yy67e09.s1 Homo sapiens cDNA clone 278632 3'), R88485 (ym94e01.r1 Homo sapiens cDNA clone 166584 5'), and T26592 (AB329E6R Homo sapiens cDNA clone LLAB329E6 5'). Based upon sequence similarity, nh328_5 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of nh328_5 indicates that it may contain some GAA/TIGGER repeat sequences.

nh328_5 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 70 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "nm214_3"

A polynucleotide of the present invention has been identified as clone "nm214_3". nm214_3 was isolated from a human adult blood (erythroleukemia TF-1) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nm214_3

is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nm214_3 protein").

The nucleotide sequence of nm214_3 as presently determined is reported in SEQ ID NO:95, and includes a poly(A) tail. What applicants presently believe to be the proper
5 reading frame and the predicted amino acid sequence of the nm214_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:96.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nm214_3 should be approximately 1300 bp.

The nucleotide sequence disclosed herein for nm214_3 was searched against the
10 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nm214_3 demonstrated at least some similarity with sequences identified as D10083 (Human RGH1 gene), D11078 (Human RGH2 gene), R68638 (y106g11.s1 Homo sapiens cDNA clone 1385003'), U88895 (Human endogenous retrovirus H D1 leader region/integrase-derived ORF1, ORF2, and putative envelope protein
15 mRNA, complete cds), Z95327 (Human DNA sequence ***SEQUENCING IN PROGRESS *** from clone 347M6; HTGS phase 1), and Z97183 (Human DNA sequence ***SEQUENCING IN PROGRESS *** from clone ICB2046; HTGS phase 1). The predicted amino acid sequence disclosed herein for nm214_3 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The
20 predicted nm214_3 protein demonstrated at least some similarity to sequences identified as U88895 (HERV-H integrase/envelope region [Homo sapiens]). Based upon sequence similarity, nm214_3 proteins and each similar protein or peptide may share at least some activity. The nm214_3 protein has a putative signal sequence at amino acids 13 to 25 of SEQ ID NO:96, with the mature protein starting at amino acid 26. The TopPredII
25 computer program predicts a potential transmembrane domain within the nm214_3 protein sequence centered around amino acid 90 of SEQ ID NO:96.

nm214_3 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 13 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

30

Clone "nn320_2"

A polynucleotide of the present invention has been identified as clone "nn320_2". nn320_2 was isolated from a human fetal kidney (293 cell line) cDNA library using

methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nn320_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nn320_2 protein").

The nucleotide sequence of nn320_2 as presently determined is reported in SEQ ID NO:97, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nn320_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:98. Amino acids 4 to 16 of SEQ ID NO:98 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 17. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nn320_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nn320_2 should be approximately 2500 bp.

The nucleotide sequence disclosed herein for nn320_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nn320_2 demonstrated at least some similarity with sequences identified as AA423969 (zv79h04.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 759895 5') and AA423988 (zv79h04.s1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 759895 3'). The predicted amino acid sequence disclosed herein for nn320_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nn320_2 protein demonstrated at least some similarity to sequences identified as M60351 (filamentous hemagglutinin [Bordetella pertussis]) and R05041 (Filamentous haemagglutinin A). The predicted nn320_2 protein also demonstrated similarity to a variety of proteases and enzyme precursors such as trypsinogen precursor. Based upon sequence similarity, nn320_2 proteins and each similar protein or peptide may share at least some activity.

nn320_2 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 58 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "pp392_3"

A polynucleotide of the present invention has been identified as clone "pp392_3". pp392_3 was isolated from a human adult blood (lymphoblastic leukemia MOLT-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins
5 (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pp392_3 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pp392_3 protein").

The nucleotide sequence of pp392_3 as presently determined is reported in SEQ
10 ID NO:99, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pp392_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:100.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pp392_3 should be approximately 2100 bp.

15 The nucleotide sequence disclosed herein for pp392_3 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pp392_3 demonstrated at least some similarity with sequences identified as AA117686 (mo64c07.r1 Stratagene mouse heart (#937316) Mus musculus cDNA clone 558348 5') and AL008726 (Human DNA sequence *** SEQUENCING IN
20 PROGRESS *** from clone 337O18; HTGS phase 1). Based upon sequence similarity, pp392_3 proteins and each similar protein or peptide may share at least some activity. The pp392_3 protein has a putative signal sequence at amino acids 196 to 208 of SEQ ID NO:100, with the mature protein starting at amino acid 209. The TopPredII computer program predicts three potential transmembrane domains within the pp392_3 protein
25 sequence centered around amino acids 20, 130, and 310 of SEQ ID NO:100, respectively.

The nucleotide sequence of pp392_3 indicates that it may contain a CA repetitive element.

pp392_3 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 56 kDa was detected in membrane fractions using SDS
30 polyacrylamide gel electrophoresis.

Clone "ya13_1"

A polynucleotide of the present invention has been identified as clone "ya13_1". ya13_1 was isolated from a human adult testes cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ya13_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ya13_1 protein").

The nucleotide sequence of ya13_1 as presently determined is reported in SEQ ID NO:101, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ya13_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:102. Amino acids 72 to 84 of SEQ ID NO:102 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 85. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ya13_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ya13_1 should be approximately 750 bp.

The nucleotide sequence disclosed herein for ya13_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ya13_1 demonstrated at least some similarity with sequences identified as AA190721 (zp88a07.r1 Stratagene HeLa cell s3 937216 Homo sapiens cDNA clone 627252 5'). Based upon sequence similarity, ya13_1 proteins and each similar protein or peptide may share at least some activity.

Clone "yb37_1"

A polynucleotide of the present invention has been identified as clone "yb37_1". yb37_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb37_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb37_1 protein").

The nucleotide sequence of yb37_1 as presently determined is reported in SEQ ID NO:103, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb37_1 protein

corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:104. Amino acids 28 to 40 of SEQ ID NO:104 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 41. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb37_1 protein. The TopPredII computer program predicts an additional potential transmembrane domain within the yb37_1 protein sequence centered around amino acid 144 of SEQ ID NO:104.

Another possible reading frame and predicted amino acid sequence encoded by yb37_1 is reported in SEQ ID NO:275; amino acids 49 to 61 of SEQ ID NO:275 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 62. Due to the hydrophobic nature of this predicted leader/signal sequence, it is likely to act as a transmembrane domain should it not be separated from the remainder of the protein of SEQ ID NO:275.

The nucleotide sequence disclosed herein for yb37_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No hits were found in the database. The nucleotide sequence of yb37_1 indicates that it may contain one or more A/TAAA repetitive elements.

yb37_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 33 kDa was detected in conditioned medium fractions using SDS polyacrylamide gel electrophoresis.

Clone "yb39_1"

A polynucleotide of the present invention has been identified as clone "yb39_1". yb39_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb39_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb39_1 protein").

The nucleotide sequence of yb39_1 as presently determined is reported in SEQ ID NO:105, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb39_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:106. Amino acids 21 to 33 of SEQ ID NO:106 are a predicted leader/signal sequence, with the

predicted mature amino acid sequence beginning at amino acid 34. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb39_1 protein.

5 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb39_1 should be approximately 825 bp.

The nucleotide sequence disclosed herein for yb39_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No hits were found in the database.

10

Clone "bd577_1"

A polynucleotide of the present invention has been identified as clone "bd577_1". bd577_1 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was
15 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bd577_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bd577_1 protein").

The nucleotide sequence of bd577_1 as presently determined is reported in SEQ
20 ID NO:107, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bd577_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:108. Amino acids 42 to 54 of SEQ ID NO:108 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 55. Due to the
25 hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bd577_1 protein.

Another possible reading frame and predicted amino acid sequence encoded by base pairs 23 to 412 of bd577_1 SEQ ID NO:107 is reported in SEQ ID NO:276; the amino
30 acid sequence of SEQ ID NO:276 has a possible signal sequence from amino acids 57 to 69, with the predicted mature amino acid sequence beginning at amino acid 70. The open reading frames corresponding to SEQ ID NO:276 and SEQ ID NO:108 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:107.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bd577_1 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for bd577_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bd577_1 demonstrated at least some similarity with sequences identified as AA306618 (EST177563 Jurkat T-cells VI Homo sapiens cDNA 5' end) and R20055 (yg39b06.r1 Homo sapiens cDNA clone 348055'). Based upon sequence similarity, bd577_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within the bd577_1 protein sequence centered around amino acids 42 and 230 of SEQ ID NO:108.

bd577_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 56 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

15 Clone "bv280_3"

A polynucleotide of the present invention has been identified as clone "bv280_3". bv280_3 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bv280_3 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "bv280_3 protein").

The nucleotide sequence of bv280_3 as presently determined is reported in SEQ ID NO:109, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bv280_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:110. Amino acids 10 to 22 of SEQ ID NO:110 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 23. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bv280_3 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bv280_3 should be approximately 1900 bp.

The nucleotide sequence disclosed herein for bv280_3 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bv280_3 demonstrated at least some similarity with sequences identified as AA095665 (15468.seq.F Fetal heart, Lambda ZAP Express Homo sapiens cDNA 5'), AA577430 (nm96g10.s1 NCI_CGAP_Co9 Homo sapiens cDNA clone IMAGE:1076130 similar to TR:G945383 G945383 CARBOXYPEPTIDASE), F06654 (H. sapiens partial cDNA sequence; clone c-1ga12), F08501 (H. sapiens partial cDNA), and H10119 (ym03f03.r1 Homo sapiens cDNA clone 46734 5' similar to SP:A41612 A41612 VITELLOGENIC CARBOXYPEPTIDASE). The predicted amino acid sequence disclosed herein for bv280_3 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted bv280_3 protein demonstrated at least some similarity to sequences identified as L46594 (carboxypeptidase [Aedes aegypti]) and R96737 (A. niger Bo-1 carboxypeptidase Y). Based upon sequence similarity, bv280_3 proteins and each similar protein or peptide may share at least some activity. The bv280_3 protein also has a serine carboxypeptidase active site motif (residues 195-212). This motif is highly specific to serine carboxypeptidases and is not found in any other type of protein in the Swiss-Prot database. The bv280_3 protein also has one copy of the crystallins beta and gamma 'Greek key' motif signature. The TopPredII computer program predicts another potential transmembrane domain within the bv280_3 protein sequence centered around amino acid 110 of SEQ ID NO:110.

bv280_3 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 61 kDa was detected in conditioned medium fractions using SDS polyacrylamide gel electrophoresis.

Clone "co315_3"

A polynucleotide of the present invention has been identified as clone "co315_3". co315_3 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. co315_3 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "co315_3 protein").

The nucleotide sequence of co315_3 as presently determined is reported in SEQ ID NO:111, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the co315_3 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:112.

- 5 Amino acids 51 to 63 of SEQ ID NO:112 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 64. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the co315_3 protein.

- 10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone co315_3 should be approximately 710 bp.

- The nucleotide sequence disclosed herein for co315_3 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. co315_3 demonstrated at least some similarity with sequences
- 15 identified as AA031371 (zk15e11.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 470636 3'), AA026051 (ze86a07.s1 Soares fetal heart NbHH19W Homo sapiens), AA393961 (zt78b10.r1 Soares testis NHT Homo sapiens cDNA clone 728443 5'), AA481047 (aa29c06.s1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:814666 3'), H46323 (yo15c05.r1 Homo sapiens cDNA clone 177992 5'), N23329 (yx78h09.s1 Homo sapiens
- 20 cDNA clone 267905 3'), and R43942 (yg22f02.s1 Homo sapiens cDNA clone 33080 3' similar to gb:M14648 VITRONECTIN RECEPTOR ALPHA SUBUNIT PRECURSOR (HUMAN)). Based upon sequence similarity, co315_3 proteins and each similar protein or peptide may share at least some activity.

- 25 Clone "ij226_6"

A polynucleotide of the present invention has a nucleotide sequence as follows:

The nucleotide sequence of ij226_6 as presently determined is reported in SEQ ID NO:113, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ij226_6 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:114.

5 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ij226_6 should be approximately 2300 bp.

The nucleotide sequence disclosed herein for ij226_6 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ij226_6 demonstrated at least some similarity with sequences
10 identified as AE000658 (Homo sapiens T-cell receptor alpha delta locus from bases 1 to 250529 (section 1 of 5) of the Complete Nucleotide Sequence), AF004231 (Homo sapiens monocyte/macrophage Ig-related receptor MIR-10 (MIR cl-10) mRNA, complete cds), G35352 (STS h14a108 5), H54023 (yq88h01.s1 Homo sapiens cDNA), H54181 (yq88h01.r1 Homo sapiens cDNA clone 202897 5'), T18551 (Human polycystic kidney disease normal
15 PKD1 gene), and Z82206 (Human DNA sequence *** SEQUENCING IN PROGRESS *** from clone 370M22; HTGS phase 1). The predicted amino acid sequence disclosed herein for ij226_6 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted ij226_6 protein demonstrated at least some similarity to sequences identified as M22334 (unknown protein [Homo
20 sapiens]). Based upon sequence similarity, ij226_6 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within the ij226_6 protein sequence centered around amino acids 37 and 62 of SEQ ID NO:114. The nucleotide sequence of ij226_6 indicates that it may contain one or more of the following repetitive elements: L1, Alu, SVA.

25

Clone "nf443_1"

A polynucleotide of the present invention has been identified as clone "nf443_1". nf443_1 was isolated from a human adult brain (substantia nigra) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No.
30 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nf443_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nf443_1 protein").

The nucleotide sequence of nf443_1 as presently determined is reported in SEQ ID NO:115, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nf443_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:116.

5 Amino acids 21 to 43 of SEQ ID NO:116 are a possible leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 44. Due to the hydrophobic nature of this possible leader/signal sequence, it is likely to act as a transmembrane domain should the leader/signal sequence not be separated from the remainder of the nf443_1 protein.

10 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nf443_1 should be approximately 3800 bp.

The nucleotide sequence disclosed herein for nf443_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nf443_1 demonstrated at least some similarity with sequences
15 identified as AA417092 (zu07a12.s1 Soares testis NHT Homo sapiens cDNA clone 731134 3'), AA421511 (zu07a12.r1 Soares testis NHT Homo sapiens cDNA clone 731134 5'), T23707 (Human gene signature HUMGS05583), and U61233 (Bos taurus tubulin-folding cofactor D mRNA, complete cds). The predicted amino acid sequence disclosed herein for nf443_1 was searched against the GenPept and GeneSeq amino acid sequence
20 databases using the BLASTX search protocol. The predicted nf443_1 protein demonstrated at least some similarity to sequences identified as U61233 (cofactor D [Bos taurus]). Based upon sequence similarity, nf443_1 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of nf443_1 indicates that it may contain an Alu repetitive element.

25 nf443_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 10 kDa was detected in conditioned medium fractions using SDS polyacrylamide gel electrophoresis.

Clone "nt429_1"

30 A polynucleotide of the present invention has been identified as clone "nt429_1". nt429_1 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis

of computer analysis of the amino acid sequence of the encoded protein. nt429_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nt429_1 protein").

The nucleotide sequence of nt429_1 as presently determined is reported in SEQ ID NO:117, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nt429_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:118. Another possible reading frame and predicted amino acid sequence, encoded by base pairs 399 to 731 of nt429_1 SEQ ID NO:117, is reported in SEQ ID NO:277; the amino acid sequence of SEQ ID NO:277 is hydrophobic in nature near its carboxyl terminus. The overlapping open reading frames corresponding to SEQ ID NO:118 and SEQ ID NO:277 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:117.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nt429_1 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for nt429_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No significant hits were found in the database. The nucleotide sequence of nt429_1 indicates that it may contain one or more of the following repetitive elements: Alu, SVA, A.

Clone "pe503_1"

A polynucleotide of the present invention has been identified as clone "pe503_1". pe503_1 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe503_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pe503_1 protein").

The nucleotide sequence of pe503_1 as presently determined is reported in SEQ ID NO:119, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe503_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:120.

Amino acids 79 to 91 of SEQ ID NO:120 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 92. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated
5 from the remainder of the pe503_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe503_1 should be approximately 1300 bp.

The nucleotide sequence disclosed herein for pe503_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
10 FASTA search protocols. pe503_1 demonstrated at least some similarity with sequences identified as AA298572 (EST114204 HSC172 cells I Homo sapiens cDNA 5' end), AA595242 (no33a12.s1 NCI_CGAP_Pr23 Homo sapiens cDNA clone IMAGE:1102462), H60941 (yr14g06.r1 Homo sapiens cDNA clone 205306 5'), H75686 (yr77g08.r1 Homo sapiens cDNA clone 211358 5'), and R61206 (yh06d11.r1 Homo sapiens cDNA clone 42649
15 5'). Based upon sequence similarity, pe503_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four potential transmembrane domains within the pe503_1 protein sequence centered around amino acids 50, 84, 107, and 148 of SEQ ID NO:120, respectively.

pe503_1 protein was expressed in a COS cell expression system, and an expressed
20 protein band of approximately 19 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "pe834_6"

A polynucleotide of the present invention has been identified as clone "pe834_6".
25 pe834_6 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe834_6 is a full-length clone, including the entire coding sequence of a secreted
30 protein (also referred to herein as "pe834_6 protein").

The nucleotide sequence of pe834_6 as presently determined is reported in SEQ ID NO:121, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe834_6 protein

corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:122. Another possible reading frame and predicted amino acid sequence, encoded by base pairs 414 to 725 of pe834_6 SEQ ID NO:121, is reported in SEQ ID NO:278; the amino acid sequence of SEQ ID NO:278 is hydrophobic in nature near its carboxyl terminus. The overlapping open reading frames corresponding to SEQ ID NO:122 and SEQ ID NO:278 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:121.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe834_6 should be approximately 1300 bp.

The nucleotide sequence disclosed herein for pe834_6 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pe834_6 demonstrated at least some similarity with sequences identified as AA054341 (zl68f04.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 509791 3'), N21462 (yx57c10.s1 Homo sapiens cDNA clone 265842 3'), N34010 (yx75g07.r1 Homo sapiens cDNA clone 267612 5'), and T90232 (ye15c09.r1 Homo sapiens cDNA clone 117808 5'). Based upon sequence similarity, pe834_6 proteins and each similar protein or peptide may share at least some activity.

pe834_6 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 17 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "ya10_1"

A polynucleotide of the present invention has been identified as clone "ya10_1". ya10_1 was isolated from a human adult testes cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ya10_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ya10_1 protein").

The nucleotide sequence of ya10_1 as presently determined is reported in SEQ ID NO:123, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ya10_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:124. Amino acids 6 to 18 of SEQ ID NO:124 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 19. Due to the

hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ya10_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing
5 clone ya10_1 should be approximately 800 bp.

The nucleotide sequence disclosed herein for ya10_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No clearly significant hits were found in these databases. BLASTX analysis of the ya10_1 protein sequence revealed some amino acid sequence
10 similarity to cystatins (cysteine protease inhibitors) of various species. Based upon this sequence similarity, ya10_1 proteins and each similar protein or peptide may share at least some activity.

Clone "yb40_1"

15 A polynucleotide of the present invention has been identified as clone "yb40_1". yb40_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb40_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb40_1 protein").

20 The nucleotide sequence of yb40_1 as presently determined is reported in SEQ ID NO:125, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb40_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:126. Amino acids 29 to 41 of SEQ ID NO:126 are a possible leader/signal sequence, with the
25 predicted mature amino acid sequence beginning at amino acid 42. Due to the hydrophobic nature of this possible leader/signal sequence, it could act as a transmembrane domain should it not be separated from the remainder of the yb40_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing
30 clone yb40_1 should be approximately 1700 bp.

The nucleotide sequence disclosed herein for yb40_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb40_1 demonstrated at least some similarity with sequences

identified as AA595189 (no32f03.s1 NCI_CGAP_Pr23 Homo sapiens cDNA clone IMAGE:1102397), R74575 (yi58d04.r1 Homo sapiens cDNA clone 143431 5'), and T25773 (Human gene signature HUMGS08001). Based upon sequence similarity, yb40_1 proteins and each similar protein or peptide may share at least some activity.

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Clone "cs756_2"

A polynucleotide of the present invention has been identified as clone "cs756_2". cs756_2 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was
10 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cs756_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cs756_2 protein").

The nucleotide sequence of cs756_2 as presently determined is reported in SEQ ID
15 NO:127, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cs756_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:128. Amino acids 211 to 223 of SEQ ID NO:128 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 224. Due to the
20 hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cs756_2 protein. The TopPredII computer program predicts a potential transmembrane domain within the cs756_2 protein sequence of SEQ ID NO:128, centered around amino acid 15 of SEQ ID NO:128; amino acids 2 to 14 of SEQ ID NO:128
25 are also a possible leader/signal sequence, with the predicted mature amino acid sequence in that case beginning at amino acid 15.

Another possible cs756_2 reading frame and predicted amino acid sequence, encoded by base pairs 385 to 825 of SEQ ID NO:127, is reported in SEQ ID NO:279; the TopPredII computer program predicts a potential transmembrane domain centered
30 around amino acid 100 of SEQ ID NO:279. The open reading frames corresponding to SEQ ID NO:279 and SEQ ID NO:128 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:127.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cs756_2 should be approximately 3000 bp.

The nucleotide sequence disclosed herein for cs756_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cs756_2 demonstrated at least some similarity with sequences identified as AA398077 (zt58c03.s1 Soares testis NHT Homo sapiens cDNA clone 726532 3'), AA541286 (nf97e03.s1 NCI_CGAP_Co3 Homo sapiens cDNA clone IMAGE:927868), W28620 (49c2 Human retina cDNA randomly primed sublibrary Homo sapiens cDNA), and W47601 (zc35g08.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 324350 5'). The predicted amino acid sequence disclosed herein for SEQ ID NO:279 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted SEQ ID NO:279 protein demonstrated at least some similarity to sequences identified as L76938 (Werner syndrome gene, complete cds [Homo sapiens]). "Werner's syndrome (WS) is an inherited disease with clinical symptoms resembling premature aging ... [the] predicted protein is 1432 amino acids in length and shows significant similarity to DNA helicases" (Yu *et al.*, 1996, *Science* 272(5259):258-262, which is incorporated by reference herein). Based upon sequence similarity, cs756_2 proteins and each similar protein or peptide may share at least some activity. The nucleotide sequence of cs756_2 indicates that it may contain one or more of the following repetitive elements: MIR, MER.

Clone "ew150_1"

A polynucleotide of the present invention has been identified as clone "ew150_1". ew150_1 was isolated from a human adult placenta cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ew150_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ew150_1 protein").

The nucleotide sequence of ew150_1 as presently determined is reported in SEQ ID NO:129, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ew150_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:130.

Amino acids 26 to 38 of SEQ ID NO:130 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 39. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated
5 from the remainder of the ew150_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ew150_1 should be approximately 2000 bp.

The nucleotide sequence disclosed herein for ew150_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
10 FASTA search protocols. ew150_1 demonstrated at least some similarity with sequences identified as AA563938 (nk23b12.s1 NCI_CGAP_Col1 Homo sapiens cDNA clone IMAGE 1014335), D63209 (Human placenta cDNA 5'-end GEN-506F01), M90423 (Bacteriophage US3 lytic-enzyme), W23461 (zb33c01.r1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 305376 5'), and Z56916 (H.sapiens CpG DNA, clone 153b7,
15 forward read cpg153b7.ft1a). In the region around position 1514 of SEQ ID NO:129, ew150_1 also demonstrated at least some similarity with sequences encoding a mitochondrial energy-transfer proteins signature motif which is found in mitochondrial and other membrane proteins. Based upon sequence similarity, ew150_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer
20 program predicts ten potential transmembrane domains within the ew150_1 protein sequence, which are centered around amino acids 70, 106, 133, 200, 314, 349, 387, 457, 504, and 527 of SEQ ID NO:130, respectively.

Clone "gg894_13"

25 A polynucleotide of the present invention has been identified as clone "gg894_13". gg894_13 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. gg894_13 is a full-length
30 clone, including the entire coding sequence of a secreted protein (also referred to herein as "gg894_13 protein").

The nucleotide sequence of gg894_13 as presently determined is reported in SEQ ID NO:131, and includes a poly(A) tail. What applicants presently believe to be the

proper reading frame and the predicted amino acid sequence of the gg894_13 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:132. Amino acids 41 to 53 of SEQ ID NO:132 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 54. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the gg894_13 protein. Another possible gg894_13 reading frame and predicted amino acid sequence, encoded by base pairs 602 to 1129 of SEQ ID NO:131, is reported in SEQ ID NO:280. The open reading frames corresponding to SEQ ID NO:280 and SEQ ID NO:132 could be joined if a frameshift were introduced into the nucleotide sequence of SEQ ID NO:131.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone gg894_13 should be approximately 2400 bp.

The nucleotide sequence disclosed herein for gg894_13 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. gg894_13 demonstrated at least some similarity with sequences identified as H57424 (yr13a10.s1 Homo sapiens cDNA clone 205146 3'), T23885 (Human gene signature HUMGS05820), and W80358 (zh49a07.s1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 415380 3'). Based upon sequence similarity, gg894_13 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the gg894_13 protein sequence centered around amino acid 115 of SEQ ID NO:132. The nucleotide sequence of gg894_13 indicates that it may contain a RBMI repetitive element.

Clone "it217_2"

A polynucleotide of the present invention has been identified as clone "it217_2". it217_2 was isolated from a human adult brain (thalamus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. it217_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "it217_2 protein").

The nucleotide sequence of it217_2 as presently determined is reported in SEQ ID NO:133, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the it217_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:134.

5 Another possible it217_2 reading frame and predicted amino acid sequence, encoded by base pairs 45 to 311 of SEQ ID NO:133, is reported in SEQ ID NO:281. Amino acids 36 to 48 of SEQ ID NO:281 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 49. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should

10 the predicted leader/signal sequence not be separated from the remainder of the it217_2 protein. The open reading frames corresponding to SEQ ID NO:281 and SEQ ID NO:134 could be joined if at least one frameshift were introduced into the nucleotide sequence of SEQ ID NO:133.

The EcoRI/NotI restriction fragment obtainable from the deposit containing

15 clone it217_2 should be approximately 2250 bp.

The nucleotide sequence disclosed herein for it217_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. it217_2 demonstrated at least some similarity with sequences identified as AA242969 (zr65h09.r1 Soares NhHMPu S1 Homo sapiens cDNA clone

20 668321 5' similar to SW SCC2_HUMAN P48594 SQUAMOUS CELL CARCINOMA ANTIGEN 2 ;contains Alu repetitive element), B44876 (HS-1060-A1-G06-MR.abi CIT Human Genomic Sperm Library C Homo sapien genomic clone Plate CT 782 Col 11 Row M), H82168 (yv78d08.r1 Homo sapiens cDNA clone), S66896 (squamous cell carcinoma antigen), U19556 (Human squamous cell carcinoma antigen 1 (SCCA1) mRNA, complete

25 cds), U19557 (Human squamous cell carcinoma antigen 2 (SCCA2) mRNA, complete cds), and U35459 (Human bomapin mRNA, complete cds). The predicted amino acid sequence disclosed herein for it217_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted it217_2 protein demonstrated at least some similarity to sequences identified as L40377 (cytoplasmic antiproteinase 2 [Homo sapiens]), M34352 (ovalbumin [Gallus gallus]), M91161 (serpin [Equus caballus]), R25276 (SCC antigen), R48379 (Human megakaryocyte differentiation factor), S66896 (squamous cell carcinoma antigen, SCC antigen serine protease inhibitor [human, Peptide, 390 aa] [Homo sapiens]), U19568 (squamous cell carcinoma antigen

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[Homo sapiens]), and U19576 (squamous cell carcinoma antigen [Homo sapiens]). Human bomapin may play a role in the regulation of protease activities during hematopoiesis (Riewald *et al.*, 1995, *J. Biol. Chem.* 270: 26754, which is incorporated by reference herein). Serpins are SERine Proteinase INhibitors and are considered
5 extracellular in localization. Human squamous cell carcinoma antigen (SSCA) is a member of the serpin family of proteinase inhibitors, purified from sera of cancer patients. Based upon sequence similarity, it217_2 proteins and each similar protein or peptide may share at least some activity.

10 Clone "ml235_2"

A polynucleotide of the present invention has been identified as clone "ml235_2". ml235_2 was isolated from a human adult brain (caudate nucleus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis
15 of computer analysis of the amino acid sequence of the encoded protein. ml235_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "ml235_2 protein").

The nucleotide sequence of ml235_2 as presently determined is reported in SEQ ID NO:135, and includes a poly(A) tail. What applicants presently believe to be the
20 proper reading frame and the predicted amino acid sequence of the ml235_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:136. Amino acids 3 to 15 of SEQ ID NO:136 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 16. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a
25 transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the ml235_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ml235_2 should be approximately 1400 bp.

The nucleotide sequence disclosed herein for ml235_2 was searched against the
30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. ml235_2 demonstrated at least some similarity with sequences identified as AA160887 (zo79b05.s1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 593073 3'), R14349 (yf79f12.r1 Homo sapiens cDNA clone 28451 5'), and R54256

(yg74f07.r1 Homo sapiens cDNA clone 39059 5'). Based upon sequence similarity, ml235_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the ml235_2 protein sequence centered around amino acid 25 of SEQ ID NO:136.

5

Clone "mt24_2"

A polynucleotide of the present invention has been identified as clone "mt24_2". mt24_2 was isolated from a human adult testes cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was
10 identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. mt24_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "mt24_2 protein").

The nucleotide sequence of mt24_2 as presently determined is reported in SEQ ID
15 NO:137, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the mt24_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:138. Amino acids 30 to 42 of SEQ ID NO:138 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 43. Due to the
20 hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the mt24_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone mt24_2 should be approximately 1400 bp.

25 The nucleotide sequence disclosed herein for mt24_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. mt24_2 demonstrated at least some similarity with sequences identified as AA062589 (zf68f04.r1 Soares pineal gland N3HPG Homo sapiens cDNA clone 382111 5') and T19332 (b08016t Testis 1 Homo sapiens cDNA clone b08016 5' end).
30 Based upon sequence similarity, mt24_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts four potential transmembrane domains within the mt24_2 protein sequence centered around amino acids 38, 153, 167, and 232 of SEQ ID NO:138, respectively.

Clone "pe584_2"

A polynucleotide of the present invention has been identified as clone "pe584_2". pe584_2 was isolated from a human adult blood (chronic myelogenous leukemia K5) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pe584_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pe584_2 protein").

The nucleotide sequence of pe584_2 as presently determined is reported in SEQ ID NO:139, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pe584_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:140. Amino acids 27 to 39 of SEQ ID NO:140 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 40. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pe584_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pe584_2 should be approximately 3000 bp.

The nucleotide sequence disclosed herein for pe584_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pe584_2 demonstrated at least some similarity with sequences identified as AA303149 (EST13039 Uterus tumor I), AA405004 (zt06e03.s1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE 712348 3'), AA481230 (aa34g01.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone 815184 5' similar to SW TCR2_ECOLI P02981 TETRACYCLINE RESISTANCE PROTEIN), D88315 (Mouse mRNA for tetracycline transporter-like protein, complete cds), and T10077 (seq1295 Homo sapiens cDNA clone b4HB3MA-COT8-HAP-Ft109 5'). The predicted amino acid sequence disclosed herein for pe584_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted pe584_2 protein demonstrated at least some similarity to sequences identified as D88315 (tetracycline transporter-like protein [Mus musculus]). Mouse tetracycline transporter-like protein is a sugar transporter (Matsuo *et al.*, 1997, *Biochem. Biophys. Res. Comm.* 238: 126-192, which

is incorporated by reference herein). Based upon sequence similarity, pe584_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts eleven potential transmembrane domains within the pe584_2 protein sequence, which are centered around amino acids 32, 55, 78, 114, 142, 196, 235, 264, 287, 332, and 375 of SEQ ID NO:140, respectively.

Clone "pj323_2"

A polynucleotide of the present invention has been identified as clone "pj323_2". pj323_2 was isolated from a human fetal carcinoma (NTD2 cells treated with retinoic acid for 23 days) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pj323_2 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pj323_2 protein").

The nucleotide sequence of pj323_2 as presently determined is reported in SEQ ID NO:141, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pj323_2 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:142. Amino acids 150 to 162 of SEQ ID NO:142 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 163. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pj323_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pj323_2 should be approximately 2500 bp.

The nucleotide sequence disclosed herein for pj323_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pj323_2 demonstrated at least some similarity with sequences identified as AA160454 (zo74g05.r1 Stratagene pancreas (#937208) Homo sapiens cDNA clone 592664 5'), AA398257 (zt60a08.s1 Soares testis NHT Homo sapiens cDNA clone 726710 3'), and T47284 (yb64g11.s1 Homo sapiens cDNA clone 76004 3'). The predicted amino acid sequence disclosed herein for pj323_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The

predicted pj323_2 protein demonstrated at least some similarity to human integral nuclear envelope protein, lamin B receptors from several species, and sterol reductases from several species. Lamin B receptors have hydrophobic carboxy terminal portions and hydrophilic amino terminal portions. Antibodies to lamin B receptors have been found
5 in patients with primary biliary cirrhosis. Sterol reductases demonstrate sequence similarity to the hydrophobic portions of lamin B receptors. Based upon sequence similarity, pj323_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts six potential transmembrane domains within the pj323_2 protein sequence, which are centered around amino acids 47,
10 106, 164, 187, 341, and 432 of SEQ ID NO:142, respectively.

pj323_2 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 46 kDa was detected in membrane fractions using SDS polyacrylamide gel electrophoresis.

15 Clone "yb24_1"

A polynucleotide of the present invention has been identified as clone "yb24_1". yb24_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb24_1 is a full-length clone, including the
20 entire coding sequence of a secreted protein (also referred to herein as "yb24_1 protein").

The nucleotide sequence of yb24_1 as presently determined is reported in SEQ ID NO:143, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb24_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:144.
25 Amino acids 25 to 37 of SEQ ID NO:144 are a predicted leader/signal sequence with the

FASTA search protocols. yb24_1 demonstrated at least some similarity with sequences identified as AA149807 (z147c09.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 505072 3') and AB003515 (Rat mRNA for GEF-2, complete cds). Based upon sequence similarity, yb24_1 proteins and each similar protein or peptide may share at least some activity.

Clone "yb44_1"

A polynucleotide of the present invention has been identified as clone "yb44_1". yb44_1 was isolated from a human fetal brain cDNA library and was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. yb44_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "yb44_1 protein").

The nucleotide sequence of yb44_1 as presently determined is reported in SEQ ID NO:145, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the yb44_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:146. Amino acids 10 to 22 of SEQ ID NO:146 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 23. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the yb44_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone yb44_1 should be approximately 2000 bp.

The nucleotide sequence disclosed herein for yb44_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. yb44_1 demonstrated at least some similarity with sequences identified as AC000016 (***) SEQUENCING IN PROGRESS (***) EPM1/APECED region of chromosome 21, BAC clone B4P3; HTGS phase 1, 10 unordered pieces). The predicted amino acid sequence disclosed herein for yb44_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted yb44_1 protein demonstrated at least some similarity to sequences identified as R72377 (Human auxillary cytochrome P450 species 2D6 variant 2 protein) and U44753 (cytochrome P450 [Drosophila melanogaster]). Based upon sequence similarity, yb44_1

proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three additional potential transmembrane domains within the yb44_1 protein sequence, which are centered around amino acids 82, 128, and 361 of SEQ ID NO:146, respectively. The nucleotide sequence of yb44_1 indicates that it
5 may contain one or more of the following repetitive elements: Alu, AT, TATACA, MER44A, TACA.

Clone "bn69_15"

A polynucleotide of the present invention has been identified as clone "bn69_15".
10 bn69_15 was isolated from a human adult placenta cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. bn69_15 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein
15 as "bn69_15 protein").

The nucleotide sequence of bn69_15 as presently determined is reported in SEQ ID NO:147, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the bn69_15 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:148.
20 Amino acids 47 to 59 of SEQ ID NO:148 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 60. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the bn69_15 protein. Another potential bn69_15 reading frame and
25 predicted amino acid sequence is encoded by basepairs 1008 to 1352 of SEQ ID NO:147 and is reported in SEQ ID NO:282.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone bn69_15 should be approximately 2800 bp.

The nucleotide sequence disclosed herein for bn69_15 was searched against the
30 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. bn69_15 demonstrated at least some similarity with sequences identified as H80692 (yv01b10.r1 Homo sapiens cDNA clone 241435 5'), T64701 (yc48d02.r1 Homo sapiens cDNA clone 83907 5'), and W21368 (zb59c01.r1 Soares fetal

lung NbHL19W Homo sapiens cDNA clone 307872 5' similar to gb:M83186 CYTOCHROME C OXIDASE POLYPEPTIDE VIIA-HEART PRECURSOR (HUMAN)). Based upon sequence similarity, bn69_15 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts an additional
5 potential transmembrane domain within the bn69_15 protein sequence centered around amino acid 32 of SEQ ID NO:148.

Clone "cb110_1"

A polynucleotide of the present invention has been identified as clone "cb110_1".
10 cb110_1 was isolated from a human fetal brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cb110_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as
15 "cb110_1 protein").

The nucleotide sequence of cb110_1 as presently determined is reported in SEQ ID NO:149, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cb110_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:150.
20 Amino acids 36 to 48 of SEQ ID NO:150 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 49. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the cb110_1 protein.

25 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone cb110_1 should be approximately 900 bp.

The nucleotide sequence disclosed herein for cb110_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cb110_1 demonstrated at least some similarity with sequences
30 identified as AC001083 (Homo sapiens (subclone 2_a6 from BAC H75) DNA sequence, complete sequence), D28485 (Human MSMB gene for beta-microseminoprotein (MSP), promoter region and exon1), and Z98052 (Human DNA sequence *** SEQUENCING IN

PROGRESS *** from clone 505B13; HTGS phase 1). - Based upon sequence similarity, cb110_1 proteins and each similar protein or peptide may share at least some activity.

Clone "ch4_11"

5 A polynucleotide of the present invention has been identified as clone "ch4_11". ch4_11 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. ch4_11 is a full-length clone,
10 including the entire coding sequence of a secreted protein (also referred to herein as "ch4_11 protein").

The nucleotide sequence of ch4_11 as presently determined is reported in SEQ ID NO:151, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the ch4_11 protein
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:152. Amino acids 21 to 33 of SEQ ID NO:152 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 34. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated
20 from the remainder of the ch4_11 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone ch4_11 should be approximately 1600 bp.

The nucleotide sequence disclosed herein for ch4_11 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
25 FASTA search protocols. ch4_11 demonstrated at least some similarity with sequences identified as AA318160 (EST20431 Retina II Homo sapiens cDNA 5' end), R94133 (yt74g06.r1 Soares fetal liver spleen 1NFLS Homo sapiens cDNA clone 276275 5'), and W27798 (37h1 Human retina cDNA randomly primed sublibrary Homo sapiens). The predicted amino acid sequence disclosed herein for ch4_11 was searched against the
30 GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted ch4_11 protein demonstrated at least some similarity to sequences identified as L28819 (involucrin [Mus musculus]). The ch4_11 protein is the human homologue of the mouse K483_1 protein (see GenBank I80067 and I80068, GeneSeq

V09119, V09120, and W42028, and U.S. Patent No. 5,708,157). Based upon sequence similarity, ch4_11 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three potential transmembrane domains within the ch4_11 protein sequence centered around amino acids 28, 189, and
5 280 of SEQ ID NO:152, respectively.

Clone "cn621_8"

A polynucleotide of the present invention has been identified as clone "cn621_8". cn621_8 was isolated from a human fetal brain cDNA library using methods which are
10 selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. cn621_8 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "cn621_8 protein").

15 The nucleotide sequence of cn621_8 as presently determined is reported in SEQ ID NO:153, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the cn621_8 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:154.

The EcoRI/NotI restriction fragment obtainable from the deposit containing
20 clone cn621_8 should be approximately 3500 bp.

The nucleotide sequence disclosed herein for cn621_8 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. cn621_8 demonstrated at least some similarity with sequences identified as W18181 (IMAGE:20099 Soares infant brain 1NIB Homo sapiens cDNA clone
25 20099), W60570 (zd26g04.r1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 3418145'), W60661 (zd26g04.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone), and Z84474 (Human DNA sequence from PAC 111M5 on chromosome 6. Contains BBC1, RFP finger protein, EST, STS, tRNAs and polymorphic repeat). The predicted amino acid sequence disclosed herein for cn621_8 was searched against the GenPept and GeneSeq
30 amino acid sequence databases using the BLASTX search protocol. The predicted cn621_8 protein demonstrated at least some similarity to sequences identified as L35279 (BMP-1 [Homo sapiens]), U91963 (tollid-like (TLL) [Homo sapiens]), and X64414 (low density lipoprotein receptor [Mus musculus]). Based upon sequence similarity, cn621_8 proteins

and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts a potential transmembrane domain within the cn621_8 protein sequence centered around amino acid 220 of SEQ ID NO:154.

5 Clone "gy621_1"

A polynucleotide of the present invention has been identified as clone "gy621_1". gy621_1 was isolated from a human adult testes cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer
10 analysis of the amino acid sequence of the encoded protein. gy621_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "gy621_1 protein").

The nucleotide sequence of gy621_1 as presently determined is reported in SEQ ID NO:155, and includes a poly(A) tail. What applicants presently believe to be the
15 proper reading frame and the predicted amino acid sequence of the gy621_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:156. Amino acids 11 to 23 of SEQ ID NO:156 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 24. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a
20 transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the gy621_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone gy621_1 should be approximately 3800 bp.

The nucleotide sequence disclosed herein for gy621_1 was searched against the
25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. gy621_1 demonstrated at least some similarity with sequences identified as AA166536 (ms63h05.r1 Stratagene mouse embryonic carcinoma (#937317) Mus musculus cDNA clone 616281 5'), AA416723 (zu08a04.s1 Soares testis NHTT Homo sapiens cDNA clone 731214 3'), and AA463756 (aa07a05.r1 Soares NhHMPu S1 Homo
30 sapiens cDNA clone 812528 5'). Based upon sequence similarity, gy621_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts at least one additional potential transmembrane domains within the

gy621_1 protein sequence of SEQ ID NO:156. The nucleotide sequence of gy621_1 indicates that it may contain one or more AC1 or AC2 repetitive elements.

Clone "hb1041_2"

5 A polynucleotide of the present invention has been identified as clone "hb1041_2". hb1041_2 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. hb1041_2 is a full-length
10 clone, including the entire coding sequence of a secreted protein (also referred to herein as "hb1041_2 protein").

The nucleotide sequence of hb1041_2 as presently determined is reported in SEQ ID NO:157, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the hb1041_2 protein
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:158. Amino acids 55 to 67 of SEQ ID NO:158 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 68. Due to the hydrophobic nature of the predicted leader/signal sequence, it may act as a transmembrane domain should the predicted leader/signal sequence not be separated
20 from the remainder of the hb1041_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone hb1041_2 should be approximately 2450 bp.

The nucleotide sequence disclosed herein for hb1041_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
25 FASTA search protocols. hb1041_2 demonstrated at least some similarity with sequences identified as AA050445 (mj21c12.r1 Soares mouse embryo NbME13.5 14.5 Mus musculus cDNA clone 476758 5'), AA087161 (mo11b05.r1 Life Tech mouse embryo 105dpc 10665016 Mus musculus cDNA clone 553233 5'), and W84558 (zd89h10.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 356707 3'). The predicted amino acid sequence
30 disclosed herein for hb1041_2 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted hb1041_2 protein demonstrated at least some similarity to sequences identified as AB000459 (unnamed

protein product [Homo sapiens]). Based upon sequence similarity, hb1041_2 proteins and each similar protein or peptide may share at least some activity.

Clone "mh703_1"

5 A polynucleotide of the present invention has been identified as clone "mh703_1". mh703_1 was isolated from a human adult brain (thalamus) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. mh703_1 is a full-
10 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "mh703_1 protein").

The nucleotide sequence of mh703_1 as presently determined is reported in SEQ ID NO:159, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the mh703_1 protein
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:160.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone mh703_1 should be approximately 1700 bp.

The nucleotide sequence disclosed herein for mh703_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
20 FASTA search protocols. mh703_1 demonstrated at least some similarity with sequences identified as AA173536 (zp04e07.r1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 595428 5'), AA173577 (zp04e07.s1 Stratagene ovarian cancer (#937219) Homo sapiens cDNA clone 595428 3'), AA278788 (zs79a09.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE 703672 5' similar to TR E189399 E189399 HYPOTHETICAL 51.4 KD
25 PROTEIN), and T26646 (Human gene signature HUMGS08893). The predicted amino acid sequence disclosed herein for mh703_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted mh703_1 protein demonstrated at least some similarity to sequences identified as R85881 (WD-40 domain-contg. YCW2 protein) and U80447 (similar to the beta
30 transducin family [Caenorhabditis elegans]). mh703_1 protein contains at least two beta-transducin family Trp-Asp repeat signature motifs, and also contains the WD-40 motif of G-proteins. Based upon sequence similarity, mh703_1 proteins and each similar protein or peptide may share at least some activity.

mh703_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 51 kDa was detected in conditioned medium using SDS polyacrylamide gel electrophoresis.

5 Clone "na461_19"

A polynucleotide of the present invention has been identified as clone "na461_19". na461_19 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis
10 of computer analysis of the amino acid sequence of the encoded protein. na461_19 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na461_19 protein").

The nucleotide sequence of na461_19 as presently determined is reported in SEQ ID NO:161, and includes a poly(A) tail. What applicants presently believe to be the
15 proper reading frame and the predicted amino acid sequence of the na461_19 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:162. Amino acids 63 to 75 of SEQ ID NO:162 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 76. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a
20 transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na461_19 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na461_19 should be approximately 2300 bp.

The nucleotide sequence disclosed herein for na461_19 was searched against the
25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. na461_19 demonstrated at least some similarity with sequences identified as AA032203 (zf01d04.s1 Soares fetal heart NbHH19W Homo sapiens cDNA clone 375655 3'), AA203707 (zx52c12.r1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 446134 5' similar to contains element MER2 repetitive element), AA262333
30 (zr70h11.s1 Soares NhHMPu S1: Homo sapiens cDNA clone 668805 3'), AA318276 (EST20340 Retina II Homo sapiens cDNA 5' end), AA436588 (zv08e12.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 753070 5'), and T21229 (Human gene signature

HUMGS02545). Based upon sequence similarity, na461_19 proteins and each similar protein or peptide may share at least some activity.

Clone "na492_2"

5 A polynucleotide of the present invention has been identified as clone "na492_2". na492_2 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. na492_2 is a full-
10 length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na492_2 protein").

The nucleotide sequence of na492_2 as presently determined is reported in SEQ ID NO:163, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the na492_2 protein
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:164. Amino acids 321 to 333 of SEQ ID NO:164 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 334. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated
20 from the remainder of the na492_2 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na492_2 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for na492_2 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
25 FASTA search protocols. na492_2 demonstrated at least some similarity with sequences identified as AA514389 (nf57b05.s1 NCI_CGAP_Co3 Homo sapiens cDNA clone IMAGE:923985), H81154 (yu60f02.r1 Homo sapiens cDNA clone 230523 5'), and R89359 (yq05c05.s1 Homo sapiens cDNA clone 196040 3'). The predicted amino acid sequence disclosed herein for na492_2 was searched against the GenPept and GeneSeq amino acid
30 sequence databases using the BLASTX search protocol. The predicted na492_2 protein demonstrated at least some similarity to sequences identified as AB004534 (pi015 [Schizosaccharomyces pombe]). Based upon sequence similarity, na492_2 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer

program predicts two potential transmembrane domains within the na492_2 protein sequence, one centered around amino acid 350 and another around amino acid 370 of SEQ ID NO:164.

5 Clone "na669_10"

A polynucleotide of the present invention has been identified as clone "na669_10". na669_10 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis
10 of computer analysis of the amino acid sequence of the encoded protein. na669_10 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "na669_10 protein").

The nucleotide sequence of na669_10 as presently determined is reported in SEQ ID NO:165, and includes a poly(A) tail. What applicants presently believe to be the
15 proper reading frame and the predicted amino acid sequence of the na669_10 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:166. Amino acids 40 to 52 of SEQ ID NO:166 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 53. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a
20 transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the na669_10 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone na669_10 should be approximately 3300 bp.

The nucleotide sequence disclosed herein for na669_10 was searched against the
25 GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. na669_10 demonstrated at least some similarity with sequences identified as AA035207 (zk27h11.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 471813 3'), AA429797 (zw57d10.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 774163 5'), AA512946 (nh91d01.s1 NCI_CGAP_Br1.1 Homo sapiens cDNA
30 clone IMAGE:965857), C20746 (HUMGS0004776, Human Gene Signature), and N33343 (yy08d08.s1 Homo sapiens cDNA clone 270639 3'). Based upon sequence similarity, na669_10 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts two potential transmembrane domains within

the na669_10 protein sequence, one centered around amino acid 11 and another around amino acid 46 of SEQ ID NO:166.

Clone "co821_31"

5 A polynucleotide of the present invention has been identified as clone "co821_31". co821_31 was isolated from a human adult brain cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. co821_31 is a full-length
10 clone, including the entire coding sequence of a secreted protein (also referred to herein as "co821_31 protein").

The nucleotide sequence of co821_31 as presently determined is reported in SEQ ID NO:167, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the co821_31 protein
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:168. Amino acids 87 to 99 of SEQ ID NO:168 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 100. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated
20 from the remainder of the co821_31 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone co821_31 should be approximately 2400 bp.

The nucleotide sequence disclosed herein for co821_31 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
25 FASTA search protocols. co821_31 demonstrated at least some similarity with sequences identified as AA488906 (aa55a02.r1 NCI_CGAP_GCB1 Homo sapiens cDNA clone IMAGE:8248105' similar to TR:G607003 G607003 BETA TRANSDUCIN-LIKE PROTEIN), L26690 (Mus musculus expressed sequence tag EST F101), N30002 (yx82e02.s1 Homo sapiens cDNA clone 268250 3'), R82926 (EST23j22 Clontech adult human fat cell library
30 HL1108A Homo sapiens cDNA clone 23j22), T20673 (Human gene signature HUMGS01889), and W44749 (zb98b11.s1 Soares parathyroid tumor NbHPA Homo sapiens cDNA clone 320829 3'). The predicted amino acid sequence disclosed herein for co821_31 was searched against the GenPept and GeneSeq amino acid sequence databases

using the BLASTX search protocol. The predicted co821_31 protein demonstrated at least some similarity to sequences identified as U51030 (Ydr267cp [Saccharomyces cerevisiae]). The predicted co821_31 protein also demonstrated at least some similarity to U92792 (general transcriptional repressor Tup1 [Schizosaccharomyces pombe]), L28125 (beta transducin-like protein (het-e1) [Podospora anserina]), and other proteins containing WD-40 motifs. Based upon sequence similarity, co821_31 proteins and each similar protein or peptide may share at least some activity.

Clone "dk329_1"

10 A polynucleotide of the present invention has been identified as clone "dk329_1". dk329_1 was isolated from a human fetal kidney cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. dk329_1 is a full-length
15 clone, including the entire coding sequence of a secreted protein (also referred to herein as "dk329_1 protein").

The nucleotide sequence of dk329_1 as presently determined is reported in SEQ ID NO:169, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the dk329_1 protein
20 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:170. Amino acids 71 to 83 of SEQ ID NO:170 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 84. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated
25 from the remainder of the dk329_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone dk329_1 should be approximately 1300 bp.

The nucleotide sequence disclosed herein for dk329_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
30 FASTA search protocols. dk329_1 demonstrated at least some similarity with sequences identified as AA147429 (zo39g07.r1 Stratagene endothelial cell 937223 Homo sapiens cDNA clone 589308 5' similar to WP T14G10.6 CE06452 LEUCOCYTE SURFACE ANTIGEN CD53 LINE), AA190572 (zp42h08.r1 Stratagene muscle 937209 Homo sapiens

cDNA clone 612159 5' similar to WP T14G10.6 CE06452 LEUCOCYTE SURFACE ANTIGEN CD53 LINE), AA234042 (zr51a05.s1 Soares NhHMPu S1 Homo sapiens cDNA clone 666896 3' similar to WP:T14G10.6 CE06452 LEUCOCYTE SURFACE ANTIGEN CD53 LINE), AA236262 (zr51a05.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 5 666896 5' similar to WP:T14G10.6 CE06452 LEUCOCYTE SURFACE ANTIGEN CD53 LINE), N72328 (yv31f12.r1 Homo sapiens cDNA clone 244367 5' similar to SW A15_HUMANP41732 CELLSURFACE GLYCOPROTEIN A15), and W50192 (mb08d07.r1 Life Tech mouse brain Mus musculus cDNA clone 319597 5' similar to SW:CD53_HUMAN P19397 LEUCOCYTE SURFACE ANTIGEN CD53). The predicted 10 amino acid sequence disclosed herein for dk329_1 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted dk329_1 protein demonstrated at least some similarity to sequences identified as Z68880 (T14G10.6 [Caenorhabditis elegans]) and a variety of membrane proteins involved in immune function. Based upon sequence similarity, dk329_1 proteins and 15 each similar protein or peptide may share at least some activity. The TopPredII computer program predicts three potential transmembrane domains within the dk329_1 protein sequence, centered around amino acids 31, 71, and 103 of SEQ ID NO:170, respectively.

dk329_1 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 18 kDa was detected in membrane fractions using SDS 20 polyacrylamide gel electrophoresis.

Clone "fx317_11"

A polynucleotide of the present invention has been identified as clone "fx317_11". fx317_11 was isolated from a human fetal brain cDNA library using methods which are 25 selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. fx317_11 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "fx317_11 protein").

30 The nucleotide sequence of fx317_11 as presently determined is reported in SEQ ID NO:171, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the fx317_11 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:172.

Amino acids 229 to 241 of SEQ ID NO:172 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 242. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the fx317_11 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone fx317_11 should be approximately 1900 bp.

The nucleotide sequence disclosed herein for fx317_11 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. fx317_11 demonstrated at least some similarity with sequences identified as AA505600 (nh93h11.s1 NCI_CGAP_Br2 Homo sapiens cDNA clone IMAGE:966117), N47450 (yy89c09.r1 Homo sapiens cDNA clone 280720 5' similar to contains element PTR5 repetitive element), T64549 (Human activated platelet protein-2 APP-2 cDNA), and W52611 (zc49e02.r1 Soares senescent fibroblasts NbHSF Homo sapiens cDNA clone 325658 5'). The predicted amino acid sequence disclosed herein for fx317_11 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted fx317_11 protein demonstrated at least some similarity to sequences identified as W15413 (Human activated platelet protein-2 APP-2) and W15414 (Human activated platelet protein-2 APP-2 alternatively spliced variant). APP-2 protein is expressed on activated human platelets. Based upon sequence similarity, fx317_11 proteins and each similar protein or peptide may share at least some activity.

Clone "lp547_4"

A polynucleotide of the present invention has been identified as clone "lp547_4". lp547_4 was isolated from a human adult blood (peripheral blood mononuclear cells treated *in vivo* with granulocyte-colony stimulating factor) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. lp547_4 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "lp547_4 protein").

The nucleotide sequence of lp547_4 as presently determined is reported in SEQ ID NO:173, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the lp547_4 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:174.

5 The EcoRI/NotI restriction fragment obtainable from the deposit containing clone lp547_4 should be approximately 1800 bp.

The nucleotide sequence disclosed herein for lp547_4 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. lp547_4 demonstrated at least some similarity with sequences
10 identified as AA442560 (zv75g07.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 7595165' similar to TR:G436941 G436941 PHORBOLINI). The predicted amino acid sequence disclosed herein for lp547_4 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted lp547_4 protein demonstrated at least some similarity to sequences identified as R58704 (Apo-B
15 RNA editing protein), U03891 (phorbolin I [Homo sapiens]), and U21951 (apolipoprotein B mRNA-editing component 1 [Mus musculus]). U03891 protein (phorbolin I) is upregulated in psoriatic keratinocytes. The predicted lp547_4 protein also contains a cytidine and deoxycytidylate deaminases zinc-binding region signature. Based upon sequence similarity, lp547_4 proteins and each similar protein or peptide may share at
20 least some activity. The TopPredII computer program predicts a potential transmembrane domain within the lp547_4 protein sequence, centered around amino acid 290 of SEQ ID NO:174; amino acids 278 to 290 are also a possible leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 291.

lp547_4 protein was expressed in a COS cell expression system, and an expressed
25 protein band of approximately 41 kDa was detected in conditioned medium and membrane fractions using SDS polyacrylamide gel electrophoresis.

Clone "lv310_7"

A polynucleotide of the present invention has been identified as clone "lv310_7".
30 Clones were first isolated from a human adult thyroid cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or were identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. Probes derived

from these cDNAs were then used to isolate lv310_7 from a human adult brain cDNA library. lv310_7 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "lv310_7 protein").

The nucleotide sequence of lv310_7 as presently determined is reported in SEQ ID NO:175, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the lv310_7 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:176. Amino acids 269 to 281 of SEQ ID NO:176 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 282. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the lv310_7 protein.

Another possible lv310_7 reading frame and predicted amino acid sequence, encoded by base pairs 1619 to 2188 of SEQ ID NO:175, is reported in SEQ ID NO:283.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone lv310_7 should be approximately 3650 bp.

The nucleotide sequence disclosed herein for lv310_7 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. lv310_7 demonstrated at least some similarity with sequences identified as N37001 (yy40a01.s1 Homo sapiens cDNA clone 273672 3'), R56228 (yg90d01.s1 Homo sapiens cDNA clone 40958 3'), and R56310 (yg90d01.r1 Homo sapiens cDNA clone 40958 5'). The predicted amino acid sequence disclosed herein for lv310_7 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted lv310_7 protein demonstrated at least some similarity to sequences identified as U24223 (alpha-CP1 [Homo sapiens]). Based upon sequence similarity, lv310_7 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts 10 potential transmembrane domains within the lv310_7 protein sequence, centered around amino acids 100, 130, 160, 210, 280, 490, 520, 600, 690, and 750 of SEQ ID NO:176, respectively.

Clone "nq34_12"

A polynucleotide of the present invention has been identified as clone "nq34_12". nq34_12 was isolated from a human adult blood (erythroleukemia TF-1) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. nq34_12 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "nq34_12 protein").

The nucleotide sequence of nq34_12 as presently determined is reported in SEQ ID NO:177, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the nq34_12 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:178. Amino acids 287 to 299 of SEQ ID NO:178 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 300. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the nq34_12 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone nq34_12 should be approximately 1700 bp.

The nucleotide sequence disclosed herein for nq34_12 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. nq34_12 demonstrated at least some similarity with sequences identified as AA126375 (zl86c06.r1 Stratagene colon (#937204) Homo sapiens cDNA clone 511498 5'), AA446675 (zw84a08.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 783638 5'), AA448974 (zx07d05.r1 Soares total fetus Nb2HF8 9w Homo sapiens cDNA clone 785769 5' similar to SW YND0_YEAST P40344 HYPOTHETICAL 35.9 KD PROTEIN IN RPC34-CSE2 INTERGENIC REGION), R57902 (F6699 Fetal heart Homo sapiens cDNA clone F6699 5' end), and X07453 (Plasmodium falciparum 11-1 gene part 1). The predicted amino acid sequence disclosed herein for nq34_12 was searched against the GenPept and GeneSeq amino acid sequence databases using the BLASTX search protocol. The predicted nq34_12 protein demonstrated at least some similarity to sequences identified as X77395 (N2040 gene product [Saccharomyces cerevisiae]). Based

upon sequence similarity, nq34_12 proteins and each similar protein or peptide may share at least some activity.

nq34_12 protein was expressed in a COS cell expression system, and an expressed protein band of approximately 34 kDa was detected in membrane fractions using SDS
5 polyacrylamide gel electrophoresis.

Clone "pj154_1"

A polynucleotide of the present invention has been identified as clone "pj154_1". pj154_1 was isolated from a human fetal carcinoma (NTD2 cells treated with retinoic acid
10 for 23 days) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pj154_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pj154_1 protein").

15 The nucleotide sequence of pj154_1 as presently determined is reported in SEQ ID NO:179, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pj154_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:180. Amino acids 13 to 25 of SEQ ID NO:180 are a predicted leader/signal sequence, with the
20 predicted mature amino acid sequence beginning at amino acid 26. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pj154_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing
25 clone pj154_1 should be approximately 2300 bp.

The nucleotide sequence disclosed herein for pj154_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pj154_1 demonstrated at least some similarity with sequences identified as AA223153 (zr07g12.r1 Stratagene NT2 neuronal precursor 937230 Homo
30 sapiens cDNA clone 650854 5'), AA223170 (zr07g12.s1 Stratagene NT2 neuronal precursor 937230 Homo sapiens cDNA clone 650854 3' similar to contains Alu repetitive element), H16627 (ym26d04.r1 Homo sapiens cDNA clone 49469 5'), and Z44660 (H. sapiens partial cDNA sequence; clone c-26d11). Based upon sequence similarity, pj154_1 proteins and

each similar protein or peptide may share at least some activity. The nucleotide sequence of pj154_1 indicates that it may contain an Alu repetitive element.

Clone "pk147_1"

5 A polynucleotide of the present invention has been identified as clone "pk147_1". pk147_1 was isolated from a human fetal kidney (293 cell line) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pk147_1 is a
10 full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pk147_1 protein").

The nucleotide sequence of pk147_1 as presently determined is reported in SEQ ID NO:181, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pk147_1 protein
15 corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:182. Amino acids 16 to 28 of SEQ ID NO:182 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 29. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated
20 from the remainder of the pk147_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pk147_1 should be approximately 1600 bp.

The nucleotide sequence disclosed herein for pk147_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and
25 FASTA search protocols. pk147_1 demonstrated at least some similarity with sequences identified as AA126920 (zl23h01.s1 Soares pregnant uterus NbHPU Homo sapiens cDNA clone 502801 3'), AA406448 (zv12f07.r1 Soares NhHMPu S1 Homo sapiens cDNA clone 753445 5'), and R51886 (yg78c03.s1 Homo sapiens cDNA clone 39574 3'). Based upon sequence similarity, pk147_1 proteins and each similar protein or peptide may share at
30 least some activity. The TopPredII computer program predicts an additional potential transmembrane domain within the pk147_1 protein sequence centered around amino acid 37 of SEQ ID NO:182.

Clone "pt127_1"

A polynucleotide of the present invention has been identified as clone "pt127_1". pt127_1 was isolated from a human adult blood (lymphoblastic leukemia MOLT-4) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No. 5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. pt127_1 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "pt127_1 protein").

The nucleotide sequence of pt127_1 as presently determined is reported in SEQ ID NO:183, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the pt127_1 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:184. Amino acids 8 to 20 of SEQ ID NO:184 are a predicted leader/signal sequence, with the predicted mature amino acid sequence beginning at amino acid 21. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the pt127_1 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing clone pt127_1 should be approximately 2600 bp.

The nucleotide sequence disclosed herein for pt127_1 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. pt127_1 demonstrated at least some similarity with sequences identified as AA081843 (zn19g10.r1 Stratagene neuroepithelium NT2RAMI 937234 Homo sapiens cDNA clone 547938 5') and R39258 (yc91h08.s1 Homo sapiens cDNA clone 23514 3'). Based upon sequence similarity, pt127_1 proteins and each similar protein or peptide may share at least some activity. The TopPredII computer program predicts five additional potential transmembrane domains within the pt127_1 protein sequence centered around amino acids 60, 100, 130, 190, and 240 of SEQ ID NO:184.

Clone "qo115_13"

A polynucleotide of the present invention has been identified as clone "qo115_13". qo115_13 was isolated from a human adult brain (corpus callosum) cDNA library using methods which are selective for cDNAs encoding secreted proteins (see U.S. Pat. No.

5,536,637), or was identified as encoding a secreted or transmembrane protein on the basis of computer analysis of the amino acid sequence of the encoded protein. qo115_13 is a full-length clone, including the entire coding sequence of a secreted protein (also referred to herein as "qo115_13 protein").

5 The nucleotide sequence of qo115_13 as presently determined is reported in SEQ ID NO:185, and includes a poly(A) tail. What applicants presently believe to be the proper reading frame and the predicted amino acid sequence of the qo115_13 protein corresponding to the foregoing nucleotide sequence is reported in SEQ ID NO:186. Amino acids 29 to 41 of SEQ ID NO:186 are a predicted leader/signal sequence, with the
10 predicted mature amino acid sequence beginning at amino acid 42. Due to the hydrophobic nature of the predicted leader/signal sequence, it is likely to act as a transmembrane domain should the predicted leader/signal sequence not be separated from the remainder of the qo115_13 protein.

The EcoRI/NotI restriction fragment obtainable from the deposit containing
15 clone qo115_13 should be approximately 1200 bp.

The nucleotide sequence disclosed herein for qo115_13 was searched against the GenBank and GeneSeq nucleotide sequence databases using BLASTN/BLASTX and FASTA search protocols. No significant hits were found in the database. The nucleotide sequence of qo115_13 indicates that it may contain repetitive elements.
20

Deposit of Clones

Clones bd306_7, fj283_11, fk317_3, k213_2x, na316_1, nf93_20, np164_1, pe204_1, ya1_1, and yb8_1 were deposited on November 26, 1997 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.)
25 as an original deposit under the Budapest Treaty and were given the accession number 98599, from which each clone comprising a particular polynucleotide is obtainable. Clone fj283_6 was deposited on 17 November, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and was given the accession number 98988.
30 Clones am856_3, am996_12, cc69_1, cc162_1, if87_1, nn103_4, np206_8, nt746_4, pe286_1, and yb7_1 were deposited on December 4, 1997 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.)

as an original deposit under the Budapest Treaty and were given the accession number 98600, from which each clone comprising a particular polynucleotide is obtainable.

Clones am728_60, bf377_1, cw354_1, nm134_4, yb11_1, and yc2_1 were deposited on December 19, 1997 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98621, from which each clone comprising a particular polynucleotide is obtainable.

Clones ff168_12, ls9_1, na1010_1, nf87_1, nh796_1, nn229_1, and np156_1 were deposited on December 31, 1997 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98623, from which each clone comprising a particular polynucleotide is obtainable.

Clones bg570_1, bi120_2, bn594_1, en554_1, na474_10, nn16_10, np189_9, ny226_1, pe159_1, and pj314_8 were deposited on January 7, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98629, from which each clone comprising a particular polynucleotide is obtainable.

Clones bp870_2, bx141_2, cw272_7, nh328_5, nm214_3, nn320_2, pp392_3, ya13_1, yb37_1, and yb39_1 were deposited on January 8, 1998 with the American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98630, from which each clone comprising a particular polynucleotide is obtainable. Clone bp870_1 was deposited on April 7, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and was given the accession number 98724, from which deposit the bp870_1 clone comprising a particular polynucleotide is obtainable.

Clones bd577_1, bv280_3, co315_3, ij226_6, nf443_1, nt429_1, pe503_1, pe834_6, ya10_1, and yb40_1 were deposited on January 13, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98631, from which each clone comprising a particular polynucleotide is obtainable.

Clones cs756_2, ew150_1, gg894_13, it217_2, ml235_2, mt24_2, pe584_2, pj323_2, yb24_1, and yb44_1 were deposited on January 22, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98636, from which each clone comprising a particular polynucleotide is obtainable.

Clones bn69_15, cb110_1, ch4_11, cn621_8, gy621_1, hb1041_2, mh703_1, na461_19, na492_2, and na669_10 were deposited on January 30, 1998 with the ATCC (American Type Culture Collection, 10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number 98647, from which each clone comprising a particular polynucleotide is obtainable.

Clones co821_31, dk329_1, fx317_11, lp547_4, lv310_7, nq34_12, pj154_1, pk147_1, pt127_1, and qo115_13 were deposited on February 18, 1998 with the American Type Culture Collection (10801 University Boulevard, Manassas, Virginia 20110-2209 U.S.A.) as an original deposit under the Budapest Treaty and were given the accession number ATCC 98663, from which each clone comprising a particular polynucleotide is obtainable.

All restrictions on the availability to the public of the deposited material will be irrevocably removed upon the granting of the patent, except for the requirements specified in 37 C.F.R. § 1.808(b), and the term of the deposit will comply with 37 C.F.R. § 1.806.

Each clone has been transfected into separate bacterial cells (*E. coli*) in these composite deposits. Each clone can be removed from the vector in which it was deposited by performing an EcoRI/NotI digestion (5' site, EcoRI; 3' site, NotI) to produce the appropriate fragment for such clone. Each clone was deposited in either the pED6 or pNOTs vector depicted in Figures 1A and 1B, respectively. The pED6dpc2 vector ("pED6") was derived from pED6dpc1 by insertion of a new polylinker to facilitate cDNA cloning (Kaufman *et al.*, 1991, *Nucleic Acids Res.* 19: 4485-4490); the pNOTs vector was derived from pMT2 (Kaufman *et al.*, 1989, *Mol. Cell. Biol.* 9: 946-958) by deletion of the DHFR sequences, insertion of a new polylinker, and insertion of the M13 origin of replication in the ClaI site. In some instances, the deposited clone can become "flipped" (i.e., in the reverse orientation) in the deposited isolate. In such instances, the cDNA insert can still be isolated by digestion with EcoRI and NotI. However, NotI will then produce the 5' site and EcoRI will produce the 3' site for placement of the cDNA in proper

orientation for expression in a suitable vector. The cDNA may also be expressed from the vectors in which they were deposited.

Bacterial cells containing a particular clone can be obtained from the composite deposit as follows:

- 5 An oligonucleotide probe or probes should be designed to the sequence that is known for that particular clone. This sequence can be derived from the sequences provided herein, or from a combination of those sequences. The sequence of an oligonucleotide probe that was used to isolate or to sequence each full-length clone is identified below, and should be most reliable in isolating the clone of interest.

10	<u>Clone</u>	<u>Probe Sequence</u>
	bd306_7	SEQ ID NO:187
	fj283_11	SEQ ID NO:188
	fj283_6	SEQ ID NO:197
15	fk317_3	SEQ ID NO:189
	k213_2x	SEQ ID NO:190
	na316_1	SEQ ID NO:191
	nf93_20	SEQ ID NO:192
	np164_1	SEQ ID NO:193
20	pe204_1	SEQ ID NO:194
	ya1_1	SEQ ID NO:195
	yb8_1	SEQ ID NO:196
	am856_3	SEQ ID NO:199
	am996_12	SEQ ID NO:200
25	cc69_1	SEQ ID NO:201
	cc162_1	SEQ ID NO:202
	if87_1	SEQ ID NO:203
	nn103_4	SEQ ID NO:204
	np206_8	SEQ ID NO:205
30	nt746_4	SEQ ID NO:206
	pe286_1	SEQ ID NO:207
	yb7_1	SEQ ID NO:208
	am728_60	SEQ ID NO:209

	cw354_1	SEQ ID NO:210
	nm134_4	SEQ ID NO:211
	yb11_1	SEQ ID NO:212
	yc2_1	SEQ ID NO:213
5	ff168_12	SEQ ID NO:214
	ls9_1	SEQ ID NO:215
	na1010_1	SEQ ID NO:216
	nf87_1	SEQ ID NO:217
	nh796_1	SEQ ID NO:218
10	nn229_1	SEQ ID NO:219
	np156_1	SEQ ID NO:220
	bi120_2	SEQ ID NO:221
	na474_10	SEQ ID NO:222
	nn16_10	SEQ ID NO:223
15	np189_9	SEQ ID NO:224
	ny226_1	SEQ ID NO:225
	pe159_1	SEQ ID NO:226
	pj314_8	SEQ ID NO:227
	bp870_1	SEQ ID NO:228
20	bx141_2	SEQ ID NO:229
	cw272_7	SEQ ID NO:230
	nh328_5	SEQ ID NO:231
	nm214_3	SEQ ID NO:232
	nn320_2	SEQ ID NO:233
25	pp392_3	SEQ ID NO:234
	yb37_1	SEQ ID NO:235
	bd577_1	SEQ ID NO:236
	bv280_3	SEQ ID NO:237
	co315_3	SEQ ID NO:238
30	ij226_6	SEQ ID NO:239
	nf443_1	SEQ ID NO:240
	nt429_1	SEQ ID NO:241
	pe503_1	SEQ ID NO:242

	pe834_6	SEQ ID NO:243
	yb40_1	SEQ ID NO:244
	cs756_2	SEQ ID NO:245
	ew150_1	SEQ ID NO:246
5	gg894_13	SEQ ID NO:247
	it217_2	SEQ ID NO:248
	ml235_2	SEQ ID NO:249
	mt24_2	SEQ ID NO:250
	pe584_2	SEQ ID NO:251
10	pj323_2	SEQ ID NO:252
	yb24_1	SEQ ID NO:253
	bn69_15	SEQ ID NO:254
	cb110_1	SEQ ID NO:255
	ch4_11	SEQ ID NO:256
15	cn621_8	SEQ ID NO:257
	gy621_1	SEQ ID NO:258
	hb1041_2	SEQ ID NO:259
	mh703_1	SEQ ID NO:260
	na461_19	SEQ ID NO:261
20	na492_2	SEQ ID NO:262
	na669_10	SEQ ID NO:263
	co821_31	SEQ ID NO:264
	dk329_1	SEQ ID NO:265
	fx317_11	SEQ ID NO:266
25	lp547_4	SEQ ID NO:267
	lv310_7	SEQ ID NO:268
	nq34_12	SEQ ID NO:269
	pj154_1	SEQ ID NO:270
	pk147_1	SEQ ID NO:271
30	pt127_1	SEQ ID NO:272
	qol15_13	SEQ ID NO:273

In the sequences listed above which include an N at position 2, that position is occupied in preferred probes/primers by a biotinylated phosphoramidite residue rather than a nucleotide (such as, for example, that produced by use of biotin phosphoramidite (1-dimethoxytrityloxy-2-(N-biotinyl-4-aminobutyl)-propyl-3-O-(2-cyanoethyl)-(N,N-diisopropyl)-phosphoramidite) (Glen Research, cat. no. 10-1953)).

The design of the oligonucleotide probe should preferably follow these parameters:

- (a) It should be designed to an area of the sequence which has the fewest ambiguous bases ("N's"), if any;
- (b) It should be designed to have a T_m of approx. 80 ° C (assuming 2° for each A or T and 4 degrees for each G or C).

The oligonucleotide should preferably be labeled with γ - ^{32}P ATP (specific activity 6000 Ci/mmol) and T4 polynucleotide kinase using commonly employed techniques for labeling oligonucleotides. Other labeling techniques can also be used. Unincorporated label should preferably be removed by gel filtration chromatography or other established methods. The amount of radioactivity incorporated into the probe should be quantitated by measurement in a scintillation counter. Preferably, specific activity of the resulting probe should be approximately 4×10^6 dpm/pmol.

The bacterial culture containing the pool of full-length clones should preferably be thawed and 100 μl of the stock used to inoculate a sterile culture flask containing 25 ml of sterile L-broth containing ampicillin at 100 $\mu\text{g}/\text{ml}$. The culture should preferably be grown to saturation at 37°C, and the saturated culture should preferably be diluted in fresh L-broth. Aliquots of these dilutions should preferably be plated to determine the dilution and volume which will yield approximately 5000 distinct and well-separated colonies on solid bacteriological media containing L-broth containing ampicillin at 100 $\mu\text{g}/\text{ml}$ and agar at 1.5% in a 150 mm petri dish when grown overnight at 37°C. Other known methods of obtaining distinct, well-separated colonies can also be employed.

Standard colony hybridization procedures should then be used to transfer the colonies to nitrocellulose filters and lyse, denature and bake them.

The filter is then preferably incubated at 65°C for 1 hour with gentle agitation in 6X SSC (20X stock is 175.3 g NaCl/liter, 88.2 g Na citrate/liter, adjusted to pH 7.0 with NaOH) containing 0.5% SDS, 100 $\mu\text{g}/\text{ml}$ of yeast RNA, and 10 mM EDTA (approximately 10 mL per 150 mm filter). Preferably, the probe is then added to the hybridization mix

at a concentration greater than or equal to $1e+6$ dpm/mL. The filter is then preferably incubated at 65°C with gentle agitation overnight. The filter is then preferably washed in 500 mL of 2X SSC/0.5% SDS at room temperature without agitation, preferably followed by 500 mL of 2X SSC/0.1% SDS at room temperature with gentle shaking for 15
5 minutes. A third wash with 0.1X SSC/0.5% SDS at 65°C for 30 minutes to 1 hour is optional. The filter is then preferably dried and subjected to autoradiography for sufficient time to visualize the positives on the X-ray film. Other known hybridization methods can also be employed.

The positive colonies are picked, grown in culture, and plasmid DNA isolated
10 using standard procedures. The clones can then be verified by restriction analysis, hybridization analysis, or DNA sequencing.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example,
15 as described in H.U. Saragovi, *et al.*, Bio/Technology 10, 773-778 (1992) and in R.S. McDowell, *et al.*, J. Amer. Chem. Soc. 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites. For example, fragments of the protein may be fused through "linker"
20 sequences to the Fc portion of an immunoglobulin. For a bivalent form of the protein, such a fusion could be to the Fc portion of an IgG molecule. Other immunoglobulin isotypes may also be used to generate such fusions. For example, a protein - IgM fusion would generate a decavalent form of the protein of the invention.

The present invention also provides both full-length and mature forms of the
25 disclosed proteins. The full-length form of the such proteins is identified in the sequence listing by translation of the nucleotide sequence of each disclosed clone. The mature form(s) of such protein may be obtained by expression of the disclosed full-length polynucleotide (preferably those deposited with ATCC) in a suitable mammalian cell or other host cell. The sequence(s) of the mature form(s) of the protein may also be
30 determinable from the amino acid sequence of the full-length form.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are

derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can
5 be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of
10 the organism from which the gene was isolated.

The chromosomal location corresponding to the polynucleotide sequences disclosed herein may also be determined, for example by hybridizing appropriately labeled polynucleotides of the present invention to chromosomes *in situ*. It may also be possible to determine the corresponding chromosomal location for a disclosed
15 polynucleotide by identifying significantly similar nucleotide sequences in public databases, such as expressed sequence tags (ESTs), that have already been mapped to particular chromosomal locations. For at least some of the polynucleotide sequences disclosed herein, public database sequences having at least some similarity to the polynucleotide of the present invention have been listed by database accession number.
20 Searches using the GenBank accession numbers of these public database sequences can then be performed at an Internet site provided by the National Center for Biotechnology Information having the address <http://www.ncbi.nlm.nih.gov/UniGene/>, in order to identify "UniGene clusters" of overlapping sequences. Many of the "UniGene clusters" so identified will already have been mapped to particular chromosomal sites.

25 Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, *Trends Pharmacol. Sci.* 15(7): 250-254; Lavarosky *et al.*, 1997,
30 *Biochem. Mol. Med.* 62(1): 11-22; and Hampel, 1998, *Prog. Nucleic Acid Res. Mol. Biol.* 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are

stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein).

5 In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through insertion, preferably followed by imprecise excision, of

10 transposable elements (Plasterk, 1992, *Bioessays* 14(9): 629-633; Zwaal *et al.*, 1993, *Proc. Natl. Acad. Sci. USA* 90(16): 7431-7435; Clark *et al.*, 1994, *Proc. Natl. Acad. Sci. USA* 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour *et al.*, 1988, *Nature* 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059;

15 5,631,153; 5,614,396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the

20 protein product(s) of the corresponding gene(s).

Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms, part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and

25 transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information. For example, the TopPredII computer program can be used to predict the location of transmembrane domains in an amino acid sequence, domains which are described by the location of the center of the transmembrane domain, with at least ten transmembrane

30 amino acids on each side of the reported central residue(s).

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60%

sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

10 In particular, sequence identity may be determined using WU-BLAST (Washington University BLAST) version 2.0 software, which builds upon WU-BLAST version 1.4, which in turn is based on the public domain NCBI-BLAST version 1.4 (Altschul and Gish, 1996, Local alignment statistics, Doolittle *ed.*, *Methods in Enzymology* 266: 460-480; Altschul *et al.*, 1990, Basic local alignment search tool, *Journal of*
15 *Molecular Biology* 215: 403-410; Gish and States, 1993, Identification of protein coding regions by database similarity search, *Nature Genetics* 3: 266-272; Karlin and Altschul, 1993, Applications and statistics for multiple high-scoring segments in molecular sequences, *Proc. Natl. Acad. Sci. USA* 90: 5873-5877; all of which are incorporated by reference herein). WU-BLAST version 2.0 executable programs for several UNIX
20 platforms can be downloaded from <ftp://blast.wustl.edu/blast/executables>. The complete suite of search programs (BLASTP, BLASTN, BLASTX, TBLASTN, and TBLASTX) is provided at that site, in addition to several support programs. WU-BLAST 2.0 is copyrighted and may not be sold or redistributed in any form or manner without the express written consent of the author; but the posted executables may otherwise be freely used for
25 commercial, nonprofit, or academic purposes. In all search programs in the suite -- BLASTP, BLASTN, BLASTX, TBLASTN and TBLASTX -- the gapped alignment routines are integral to the database search itself, and thus yield much better sensitivity and selectivity while producing the more easily interpreted output. Gapping can optionally be turned off in all of these programs, if desired. The default penalty (Q) for a gap of length
30 one is Q=9 for proteins and BLASTP, and Q=10 for BLASTN, but may be changed to any integer value including zero, one through eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. The default per-residue

penalty for extending a gap (R) is $R=2$ for proteins and BLASTP, and $R=10$ for BLASTN, but may be changed to any integer value including zero, one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve through twenty, twenty-one through fifty, fifty-one through one hundred, etc. Any combination of values for Q and R can be used in order
5 to align sequences so as to maximize overlap and identity while minimizing sequence gaps. The default amino acid comparison matrix is BLOSUM62, but other amino acid comparison matrices such as PAM can be utilized.

Species homologues of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or
10 polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide. Preferably, polynucleotide species homologues have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% identity) with the given polynucleotide, and protein species homologues have at least 30% sequence
15 identity (more preferably, at least 45% identity; most preferably at least 60% identity) with the given protein, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides or the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Species homologues may be isolated and identified by making suitable probes or primers from the
20 sequences provided herein and screening a suitable nucleic acid source from the desired species. Preferably, species homologues are those isolated from mammalian species. Most preferably, species homologues are those isolated from certain mammalian species such as, for example, *Pan troglodytes*, *Gorilla gorilla*, *Pongo pygmaeus*, *Hylobates concolor*, *Macaca mulatta*, *Papio papio*, *Papio hamadryas*, *Cercopithecus aethiops*, *Cebus capucinus*, *Aotus*
25 *trivirgatus*, *Sanguinus oedipus*, *Microcebus murinus*, *Mus musculus*, *Rattus norvegicus*, *Cricetulus griseus*, *Felis catus*, *Mustela vison*, *Canis familiaris*, *Oryctolagus cuniculus*, *Bos taurus*, *Ovis aries*, *Sus scrofa*, and *Equus caballus*, for which genetic maps have been created allowing the identification of syntenic relationships between the genomic organization of genes in one species and the genomic organization of the related genes in another species
30 (O'Brien and Seuánez, 1988, *Ann. Rev. Genet.* 22: 323-351; O'Brien *et al.*, 1993, *Nature Genetics* 3:103-112; Johansson *et al.*, 1995, *Genomics* 25: 682-690; Lyons *et al.*, 1997, *Nature Genetics* 15: 47-56; O'Brien *et al.*, 1997, *Trends in Genetics* 13(10): 393-399; Carver and Stubbs, 1997, *Genome Research* 7:1123-1137; all of which are incorporated by reference herein).

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotides which also encode proteins which are identical or have significantly similar sequences to those encoded by the disclosed polynucleotides. Preferably, allelic variants have at least
5 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% identity) with the given polynucleotide, where sequence identity is determined by comparing the nucleotide sequences of the polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps. Allelic variants may be isolated and identified by making suitable probes or primers from the sequences
10 provided herein and screening a suitable nucleic acid source from individuals of the appropriate species.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides that hybridize under reduced
15 stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least
20 as stringent as, for example, conditions M-R.

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp) [†]	Hybridization Temperature and Buffer [†]	Wash Temperature and Buffer [†]
A	DNA:DNA	≥ 50	65°C; 1xSSC -or- 42°C; 1xSSC, 50% formamide	65°C; 0.3xSSC
B	DNA:DNA	<50	T _B [*] ; 1xSSC	T _B [*] ; 1xSSC
C	DNA:RNA	≥ 50	67°C; 1xSSC -or- 45°C; 1xSSC, 50% formamide	67°C; 0.3xSSC
D	DNA:RNA	<50	T _D [*] ; 1xSSC	T _D [*] ; 1xSSC
E	RNA:RNA	≥ 50	70°C; 1xSSC -or- 50°C; 1xSSC, 50% formamide	70°C; 0.3xSSC
F	RNA:RNA	<50	T _F [*] ; 1xSSC	T _F [*] ; 1xSSC
G	DNA:DNA	≥ 50	65°C; 4xSSC -or- 42°C; 4xSSC, 50% formamide	65°C; 1xSSC
H	DNA:DNA	<50	T _H [*] ; 4xSSC	T _H [*] ; 4xSSC
I	DNA:RNA	≥ 50	67°C; 4xSSC -or- 45°C; 4xSSC, 50% formamide	67°C; 1xSSC
J	DNA:RNA	<50	T _J [*] ; 4xSSC	T _J [*] ; 4xSSC
K	RNA:RNA	≥ 50	70°C; 4xSSC -or- 50°C; 4xSSC, 50% formamide	67°C; 1xSSC
L	RNA:RNA	<50	T _L [*] ; 2xSSC	T _L [*] ; 2xSSC
M	DNA:DNA	≥ 50	50°C; 4xSSC -or- 40°C; 6xSSC, 50% formamide	50°C; 2xSSC
N	DNA:DNA	<50	T _N [*] ; 6xSSC	T _N [*] ; 6xSSC
O	DNA:RNA	≥ 50	55°C; 4xSSC -or- 42°C; 6xSSC, 50% formamide	55°C; 2xSSC
P	DNA:RNA	<50	T _P [*] ; 6xSSC	T _P [*] ; 6xSSC
Q	RNA:RNA	≥ 50	60°C; 4xSSC -or- 45°C; 6xSSC, 50% formamide	60°C; 2xSSC
R	RNA:RNA	<50	T _R [*] ; 4xSSC	T _R [*] ; 4xSSC

[†]: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

[†]: SSPE (1xSSPE is 0.15M NaCl, 10mM NaH₂PO₄, and 1.25mM EDTA, pH 7.4) can be substituted for SSC (1xSSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

^{*}T_B - T_R: The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, T_m(°C) = 2(# of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T_m(°C) = 81.5 + 16.6(log₁₀[Na⁺]) + 0.41(%G+C) - (600/N), where N is the number of bases in the hybrid, and [Na⁺] is the concentration of sodium ions in the hybridization buffer ([Na⁺] for 1xSSC = 0.165 M).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and *Current Protocols in Molecular Biology*, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman *et al.*, *Nucleic Acids Res.* 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, *Methods in Enzymology* 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed (transfected) with the ligated polynucleotide/expression control sequence.

A number of types of cells may act as suitable host cells for expression of the protein. Mammalian host cells include, for example, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3 cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from *in vitro* culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or in prokaryotes such as bacteria. Potentially suitable yeast strains include *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces* strains, *Candida*, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial

strains include *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhimurium*, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, e.g., Invitrogen, San Diego, California, U.S.A. (the MaxBac® kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (i.e., from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl® or Cibacrom blue 3GA Sepharose®; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form which will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX). Kits for expression and purification of such fusion proteins are commercially available from New England BioLabs (Beverly, MA), Pharmacia (Piscataway, NJ) and Invitrogen Corporation (Carlsbad, CA), respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("Flag") is commercially available from the Eastman Kodak Company (New Haven, CT).

Finally, one or more reverse-phase high performance liquid chromatography (RP-HPLC) steps employing hydrophobic RP-HPLC media, e.g., silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to
5 provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The protein of the invention may also be expressed as a product of transgenic animals, e.g., as a component of the milk of transgenic cows, goats, pigs, or sheep which
10 are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

The protein may also be produced by known conventional chemical synthesis. Methods for constructing the proteins of the present invention by synthetic means are known to those skilled in the art. The synthetically-constructed protein sequences, by
15 virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications in the peptide or DNA sequences can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement,
20 insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, e.g., U.S. Patent No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or
25 deletion retains the desired activity of the protein.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and may thus be useful for screening or other immunological methodologies may also be easily made by those skilled in the art.

given the disclosures herein. Such modifications are believed to be encompassed by the present invention.

USES AND BIOLOGICAL ACTIVITY

5 The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors
10 suitable for introduction of DNA).

Research Uses and Utilities

 The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant
15 protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA
20 sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression
25 patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, those described in Gyuris *et al.*, 1993, *Cell* 75:
30 791-803 and in Rossi *et al.*, 1997, *Proc. Natl. Acad. Sci. USA* 94: 8405-8410, all of which are incorporated by reference herein) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may

induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK. The activity of a protein of the invention may, among other means, be measured by the following methods:

- 10 Assays for T-cell or thymocyte proliferation include without limitation those described in: *Current Protocols in Immunology*, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., *J. Immunol.* 137:3494-3500, 1986;
- 15 Bertagnolli et al., *J. Immunol.* 145:1706-1712, 1990; Bertagnolli et al., *Cellular Immunology* 133:327-341, 1991; Bertagnolli, et al., *J. Immunol.* 149:3778-3783, 1992; Bowman et al., *J. Immunol.* 152: 1756-1761, 1994.

- 20 Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ , Schreiber, R.D. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

- 25 Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., *J. Exp. Med.* 173:1205-1211, 1991; Moreau et al., *Nature* 336:690-692, 1988; Greenberger et al., *Proc. Natl. Acad. Sci. U.S.A.* 80:2931-2938, 1983;
- 30 Measurement of mouse and human interleukin 6 - Nordan, R. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., *Proc. Natl. Acad. Sci. U.S.A.* 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In *Current Protocols*

in *Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

- 5 Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience
- 10 (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

15

Immune Stimulating or Suppressing Activity

- A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies
- 20 and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral,
- 25 bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, *Leishmania* spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.
- 30 Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus,

myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to regulate immune responses in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as, for example, B7)), *e.g.*, preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (*e.g.*, B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this manner prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an

immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or
5 tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in
10 rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins *in vivo* as described in Lenschow *et al.*, Science 257:789-792 (1992) and Turka *et al.*, Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the
15 effect of blocking B lymphocyte antigen function *in vivo* on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production
20 of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which
25 may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune
30 encephalitis, systemic lupus erythematosus in MRL/*lpr/lpr* mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells *in vitro* with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the *in vitro* activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells *in vivo*.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (*e.g.*, sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected *ex vivo* with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection *in vivo*.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the

transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and β_2 microglobulin protein or an MHC class II α chain protein and an MHC class II β chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: *In vitro*

antibody production, Mond, J.J. and Brunswick, M. In *Current Protocols in Immunology*. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: *Current Protocols in Immunology*, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., *J. Immunol.* 137:3494-3500, 1986; Takai et al., *J. Immunol.* 140:508-512, 1988; Bertagnolli et al., *J. Immunol.* 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., *J. Immunol.* 134:536-544, 1995; Inaba et al., *Journal of Experimental Medicine* 173:549-559, 1991; Macatonia et al., *Journal of Immunology* 154:5071-5079, 1995; Porgador et al., *Journal of Experimental Medicine* 182:255-260, 1995; Nair et al., *Journal of Virology* 67:4062-4069, 1993; Huang et al., *Science* 264:961-965, 1994; Macatonia et al., *Journal of Experimental Medicine* 169:1255-1264, 1989; Bhardwaj et al., *Journal of Clinical Investigation* 94:797-807, 1994; and Inaba et al., *Journal of Experimental Medicine* 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., *Cytometry* 13:795-808, 1992; Gorczyca et al., *Leukemia* 7:659-670, 1993; Gorczyca et al., *Cancer Research* 53:1945-1951, 1993; Itoh et al., *Cell* 66:233-243, 1991; Zacharchuk, *Journal of Immunology* 145:4037-4045, 1990; Zamai et al., *Cytometry* 14:891-897, 1993; Gorczyca et al., *International Journal of Oncology* 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., *Blood* 84:111-117, 1994; Fine et al., *Cellular Immunology* 155:111-122, 1994; Galy et al., *Blood* 85:2770-2778, 1995; Toki et al., *Proc. Nat. Acad. Sci. USA* 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even

marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or *ex-vivo* (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama

- et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In *Culture of Hematopoietic Cells*. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

- A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

- A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. *De novo* bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

- A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors *ex vivo* for return *in vivo* to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

It is expected that a protein of the present invention may also exhibit activity for
5 generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also
10 exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting
15 differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described
20 in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in:
Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year
25 Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Activin/Inhibin Activity

A protein of the present invention may also exhibit activin- or inhibin-related
30 activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin α family, may be useful

as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- β group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

10 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., *Endocrinology* 91:562-572, 1972; Ling et al., *Nature* 321:779-782, 1986; Vale et al., *Nature* 321:776-779, 1986; Mason et al., *Nature* 318:659-663, 1985; Forage et al., *Proc.*
15 *Natl. Acad. Sci. USA* 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or
20 neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed
30 movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al. Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their

ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

10 The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and
15 Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

20 Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the
25 inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic
30 inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over

production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

Cadherin/Tumor Invasion Suppressor Activity

5 Cadherins are calcium-dependent adhesion molecules that appear to play major roles during development, particularly in defining specific cell types. Loss or alteration of normal cadherin expression can lead to changes in cell adhesion properties linked to tumor growth and metastasis. Cadherin malfunction is also implicated in other human diseases, such as pemphigus vulgaris and pemphigus foliaceus (auto-immune blistering
10 skin diseases), Crohn's disease, and some developmental abnormalities.

The cadherin superfamily includes well over forty members, each with a distinct pattern of expression. All members of the superfamily have in common conserved extracellular repeats (cadherin domains), but structural differences are found in other parts of the molecule. The cadherin domains bind calcium to form their tertiary structure and
15 thus calcium is required to mediate their adhesion. Only a few amino acids in the first cadherin domain provide the basis for homophilic adhesion; modification of this recognition site can change the specificity of a cadherin so that instead of recognizing only itself, the mutant molecule can now also bind to a different cadherin. In addition, some cadherins engage in heterophilic adhesion with other cadherins.

20 E-cadherin, one member of the cadherin superfamily, is expressed in epithelial cell types. Pathologically, if E-cadherin expression is lost in a tumor, the malignant cells become invasive and the cancer metastasizes. Transfection of cancer cell lines with polynucleotides expressing E-cadherin has reversed cancer-associated changes by returning altered cell shapes to normal, restoring cells' adhesiveness to each other and to
25 their substrate, decreasing the cell growth rate, and drastically reducing anchorage-independent cell growth. Thus, reintroducing E-cadherin expression reverts carcinomas to a less advanced stage. It is likely that other cadherins have the same invasion suppressor role in carcinomas derived from other tissue types. Therefore, proteins of the present invention with cadherin activity, and polynucleotides of the present invention
30 encoding such proteins, can be used to treat cancer. Introducing such proteins or polynucleotides into cancer cells can reduce or eliminate the cancerous changes observed in these cells by providing normal cadherin expression.

Cancer cells have also been shown to express cadherins of a different tissue type than their origin, thus allowing these cells to invade and metastasize in a different tissue in the body. Proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be substituted in these cells for the
5 inappropriately expressed cadherins, restoring normal cell adhesive properties and reducing or eliminating the tendency of the cells to metastasize.

Additionally, proteins of the present invention with cadherin activity, and polynucleotides of the present invention encoding such proteins, can be used to generate antibodies recognizing and binding to cadherins. Such antibodies can be used to block the
10 adhesion of inappropriately expressed tumor-cell cadherins, preventing the cells from forming a tumor elsewhere. Such an anti-cadherin antibody can also be used as a marker for the grade, pathological type, and prognosis of a cancer, i.e. the more progressed the cancer, the less cadherin expression there will be, and this decrease in cadherin expression can be detected by the use of a cadherin-binding antibody.

15 Fragments of proteins of the present invention with cadherin activity, preferably a polypeptide comprising a decapeptide of the cadherin recognition site, and polynucleotides of the present invention encoding such protein fragments, can also be used to block cadherin function by binding to cadherins and preventing them from binding in ways that produce undesirable effects. Additionally, fragments of proteins of the present
20 invention with cadherin activity, preferably truncated soluble cadherin fragments which have been found to be stable in the circulation of cancer patients, and polynucleotides encoding such protein fragments, can be used to disturb proper cell-cell adhesion.

Assays for cadherin adhesive and invasive suppressor activity include, without limitation, those described in: Hortsch et al. J Biol Chem 270 (32): 18809-18817, 1995;
25 Miyaki et al. Oncogene 11: 2547-2552, 1995; Ozawa et al. Cell 63: 1033-1038, 1990.

Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities.
30 A protein may inhibit tumor growth directly or indirectly (such as, for example, via antibody-dependent cell-mediated cytotoxicity (ADCC)). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by

inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth.

5 Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, 10 weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, 15 carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic 20 lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another 25 material or entity which is cross-reactive with such protein.

ADMINISTRATION AND DOSING

A protein of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources) may be used in a 30 pharmaceutical composition when combined with a pharmaceutically acceptable carrier. Such a composition may also contain (in addition to protein and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the

effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or compliment its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein of the invention, or to minimize side effects. Conversely, protein of the present invention may be included in formulations of the particular cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent.

A protein of the present invention may be active in multimers (e.g., heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunoglobulin and other molecules on B cells as well as antibodies able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other

pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithin, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent No. 4,235,871; U.S. Patent No. 4,501,728; U.S. Patent No. 4,837,028; and U.S. Patent No. 4,737,323, all of which are incorporated herein by reference.

As used herein, the term "therapeutically effective amount" means the total amount of each active component of the pharmaceutical composition or method that is sufficient to show a meaningful patient benefit, i.e., treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, the term refers to that ingredient alone. When applied to a combination, the term refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein of the present invention is administered to a mammal having a condition to be treated. Protein of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other hematopoietic factors. When co-administered with one or more cytokines, lymphokines or other hematopoietic factors, protein of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

Administration of protein of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or

cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

When a therapeutically effective amount of protein of the present invention is administered orally, protein of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein of the present invention, and preferably from about 25 to 90% protein of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein of the present invention, and preferably from about 1 to 50% protein of the present invention.

When a therapeutically effective amount of protein of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art.

The amount of protein of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein of the present invention and observe the patient's

response. Larger doses of protein of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01 μ g to about 100
5 mg (preferably about 0.1mg to about 10 mg, more preferably about 0.1 μ g to about 1 mg) of protein of the present invention per kg body weight.

The duration of intravenous therapy using the pharmaceutical composition of the present invention will vary, depending on the severity of the disease being treated and the condition and potential idiosyncratic response of each individual patient. It is
10 contemplated that the duration of each application of the protein of the present invention will be in the range of 12 to 24 hours of continuous intravenous administration. Ultimately the attending physician will decide on the appropriate duration of intravenous therapy using the pharmaceutical composition of the present invention.

Protein of the invention may also be used to immunize animals to obtain polyclonal
15 and monoclonal antibodies which specifically react with the protein. Such antibodies may be obtained using either the entire protein or fragments thereof as an immunogen. The peptide immunogens additionally may contain a cysteine residue at the carboxyl terminus, and are conjugated to a hapten such as keyhole limpet hemocyanin (KLH). Methods for synthesizing such peptides are known in the art, for example, as in R.P. Merrifield, J.
20 Amer.Chem.Soc. 85, 2149-2154 (1963); J.L. Krstenansky, *et al.*, FEBS Lett. 211, 10 (1987). Monoclonal antibodies binding to the protein of the invention may be useful diagnostic agents for the immunodetection of the protein. Neutralizing monoclonal antibodies binding to the protein may also be useful therapeutics for both conditions associated with the protein and also in the treatment of some forms of cancer where abnormal expression
25 of the protein is involved. In the case of cancerous cells or leukemic cells, neutralizing monoclonal antibodies against the protein may be useful in detecting and preventing the metastatic spread of the cancerous cells, which may be mediated by the protein.

For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the
30 composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue

damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the
5 methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

10 The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalciumphosphate, hydroxyapatite, polylactic acid, polyglycolic acid and
15 polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above mentioned types of
20 material, such as polylactic acid and hydroxyapatite or collagen and tricalciumphosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability.

Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In
25 some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose,
30 ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer

and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt%, preferably 1-10 wt% based on total formulation weight, which represents the amount necessary to prevent desorption of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells.

In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF- α and TGF- β), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins of the present invention.

The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, e.g., amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (e.g., bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either *in vivo* or *ex vivo* into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA).

Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes.

Patent and literature references cited herein are incorporated by reference as if fully set forth.

What is claimed is:

1. An isolated polynucleotide selected from the group consisting of:
 - (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1;
 - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 63 to nucleotide 1265;
 - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:1 from nucleotide 132 to nucleotide 1265;
 - (d) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone bd306_7 deposited with the ATCC under accession number 98599;
 - (e) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone bd306_7 deposited with the ATCC under accession number 98599;
 - (f) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone bd306_7 deposited with the ATCC under accession number 98599;
 - (g) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone bd306_7 deposited with the ATCC under accession number 98599;
 - (h) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2;
 - (i) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:2, the fragment comprising eight consecutive amino acids of SEQ ID NO:2; and
 - (j) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(i).
2. The polynucleotide of claim 1 wherein said polynucleotide is operably linked to at least one expression control sequence.
3. A host cell transformed with the polynucleotide of claim 2.
4. The host cell of claim 3, wherein said cell is a mammalian cell.

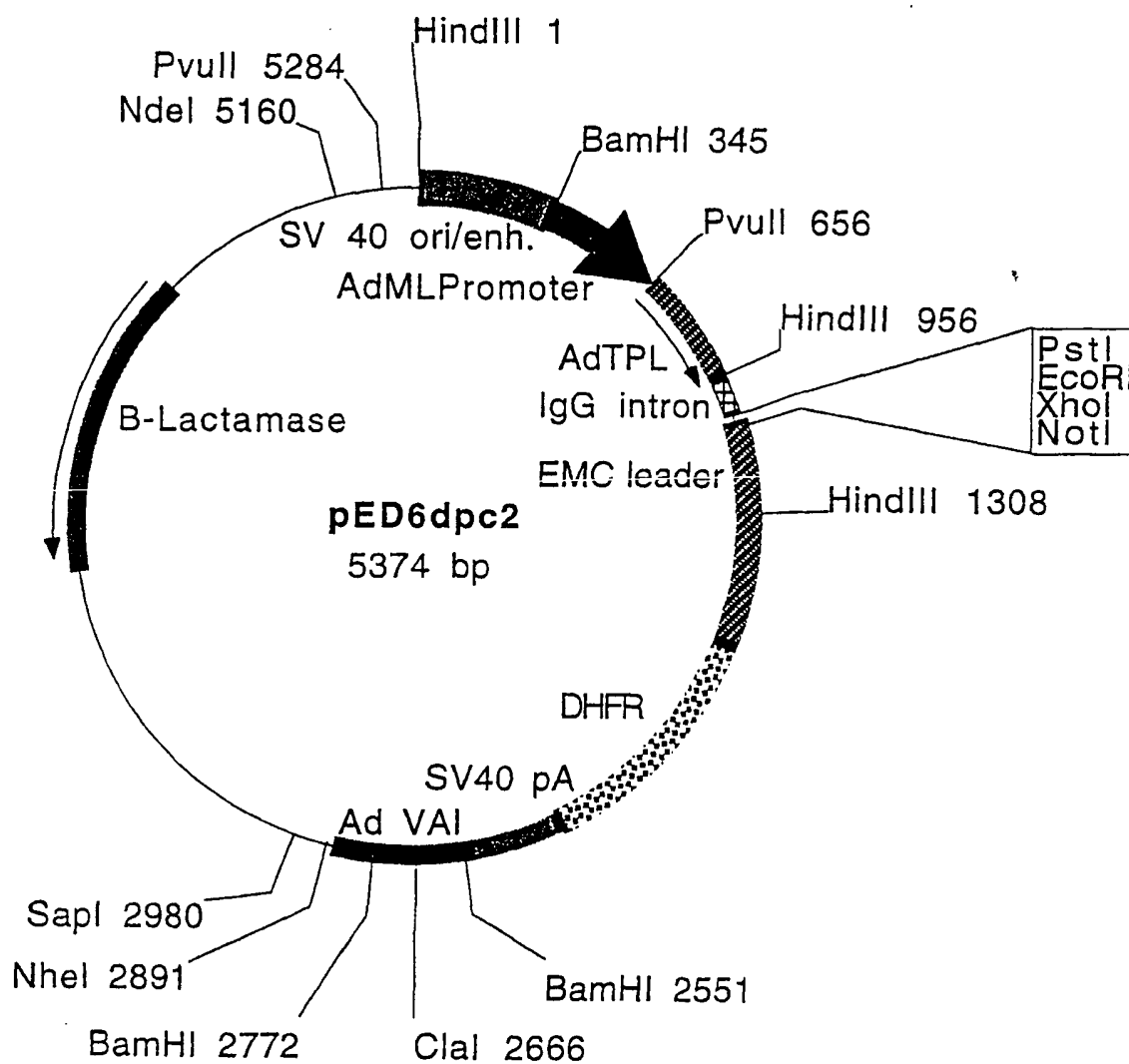
5. A process for producing a protein encoded by the polynucleotide of claim 2, which process comprises:
 - (a) growing a culture of the host cell in a suitable culture medium, wherein the host cell has been transformed with the polynucleotide of claim 2; and
 - (b) purifying said protein from the culture.
6. A protein produced according to the process of claim 5.
7. An isolated polynucleotide encoding the protein of claim 6.
8. The polynucleotide of claim 7, wherein the polynucleotide comprises the cDNA insert of clone bd306_7 deposited with the ATCC under accession number 98599.
9. A protein comprising an amino acid sequence selected from the group consisting of:
 - (a) the amino acid sequence of SEQ ID NO:2;
 - (b) the amino acid sequence of SEQ ID NO:2 from amino acid 148 to amino acid 189;
 - (c) fragments of the amino acid sequence of SEQ ID NO:2 comprising eight consecutive amino acids of SEQ ID NO:2; and
 - (d) the amino acid sequence encoded by the cDNA insert of clone bd306_7 deposited with the ATCC under accession number 98599;the protein being substantially free from other mammalian proteins.
10. The protein of claim 9, wherein said protein comprises the amino acid sequence of SEQ ID NO:2.
11. The protein of claim 9, wherein said protein comprises the amino acid sequence of SEQ ID NO:2 from amino acid 148 to amino acid 189.
12. A composition comprising the protein of claim 9 and a pharmaceutically acceptable carrier.

13. An isolated polynucleotide selected from the group consisting of:
- (a) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19;
 - (b) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 27 to nucleotide 734;
 - (c) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 270 to nucleotide 734;
 - (d) a polynucleotide comprising the nucleotide sequence of SEQ ID NO:19 from nucleotide 85 to nucleotide 1604;
 - (e) a polynucleotide comprising the nucleotide sequence of the full-length protein coding sequence of clone yb8_1 deposited under accession number ATCC 98599;
 - (f) a polynucleotide encoding the full-length protein encoded by the cDNA insert of clone yb8_1 deposited under accession number ATCC 98599;
 - (g) a polynucleotide comprising the nucleotide sequence of the mature protein coding sequence of clone yb8_1 deposited under accession number ATCC 98599;
 - (h) a polynucleotide encoding the mature protein encoded by the cDNA insert of clone yb8_1 deposited under accession number ATCC 98599;
 - (i) a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:20;
 - (j) a polynucleotide encoding a protein comprising a fragment of the amino acid sequence of SEQ ID NO:20, the fragment comprising eight consecutive amino acids of SEQ ID NO:20; and
 - (k) a polynucleotide that hybridizes under stringent conditions to any one of the polynucleotides specified in (a)-(j).
14. A protein comprising an amino acid sequence selected from the group consisting of:
- (a) the amino acid sequence of SEQ ID NO:20;
 - (b) the amino acid sequence of SEQ ID NO:20 from amino acid 70 to amino acid 236;

(c) fragments of the amino acid sequence of SEQ ID NO:20 comprising eight consecutive amino acids of SEQ ID NO:20; and

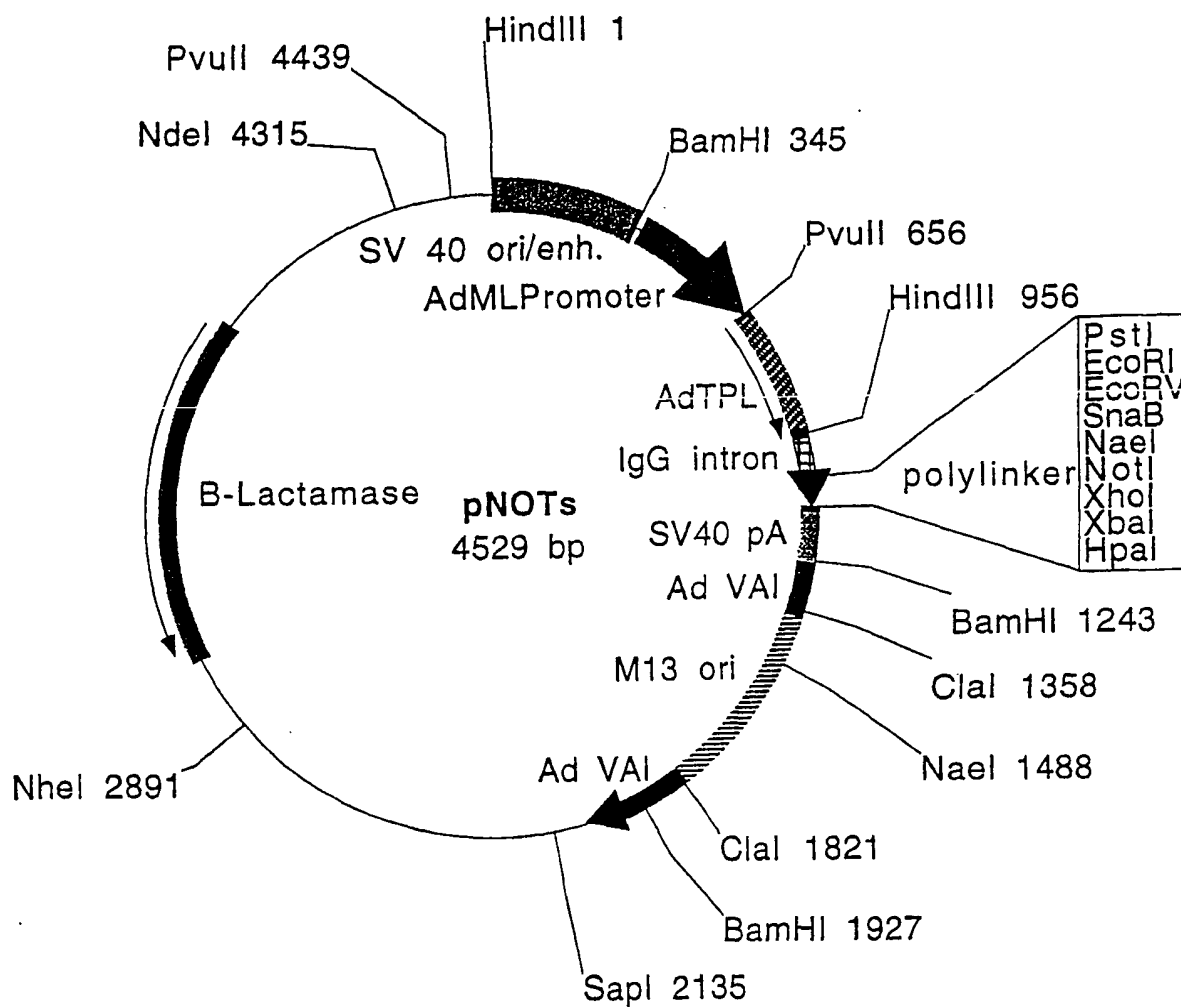
(d) the amino acid sequence encoded by the cDNA insert of clone yb8_1 deposited under accession number ATCC 98599;

the protein being substantially free from other mammalian proteins.

Fig. 1A^{1/2}

2/2

Fig. 1B



1.

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<210> 6
 <211> 122
 <212> PRT
 <213> Homo sapiens

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 Lys Thr Phe Arg Ser Gly Ala Ser Leu Gly Phe Leu His Pro Val Gln
 20 25 30
 Gln Val Leu Leu Phe Pro Phe Leu Asn Tyr Tyr Leu Leu Leu Leu Phe
 35 40 45
 Phe Glu Thr Gly Ser Pro Phe Val Thr Gln Ala Gly Met Gln Arg His
 50 55 60
 Asp His Cys Ser Leu Gln Leu Arg Pro Pro Arg Leu Lys Gly Val Ser
 65 70 75 80
 His Leu Gly Cys Cys His Thr Trp Pro Thr Phe Leu Tyr Phe Phe Gly
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<210> 7
 <211> 1969
 <212> DNA
 <213> Homo sapiens

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<210> 8
 <211> 74
 <212> PRT
 <213> Homo sapiens

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 Leu Phe Leu Ala Ser Ala Val Leu Ser Trp Lys Leu Ala Lys Met Ile
 35 40 45
 Glu Ala Arg Glu Lys Glu Gln Lys Lys Lys Gln Lys Arg Gln Glu Asn
 50 55 60
 Ile Ala Lys Ala Lys Arg Leu Lys Lys Asp
 65 70

<210> 9
 <211> 819
 <212> DNA
 <213> Homo sapiens

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 <211> 89
 <212> PRT

<213> Homo sapiens

<400> 10

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Phe Leu Leu Gln Gln Ala Ser Cys Val Cys Phe Met Ser Leu Leu Phe
 20 25 30

Cys Cys Cys Ala Leu Asn Ser Val Pro Ala Val Ser Gly Arg Leu Glu
 35 40 45

Lys Lys Ile Pro Pro Leu Lys Thr Cys Ser Leu Phe Phe Gln Ser Val
 50 55 60

Thr Pro Ala Ile Ser Leu Ala Ser His Gly Ser Val Asn Trp His Thr
 65 70 75 80

Ala Ala Val Arg Gln Trp Lys Lys Ser
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<210> 11

<211> 1969

<212> DNA

<213> Homo sapiens

<400> 11

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10

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 <211> 211
 <212> PRT
 <213> Homo sapiens

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 35 40 45
 Pro Glu Lys Cys Gln Leu Leu Phe Arg Val Ser Asp His Arg Arg Cys
 50 55 60
 Ser Gln Gly Glu Gly Ser Gln Val Gly Ser Leu Leu Ser Leu Thr Leu
 65 70 75 80
 Arg Glu Glu Phe Thr Val Leu Gly Arg Gln Val Glu Asp Ala Gly Arg
 85 90 95
 Val Leu Glu Gly Ile Ser Lys Ser Ile Ser Tyr Asp Leu Asp Gly Glu
 100 105 110
 Glu Ser Tyr Gly Lys Tyr Leu Arg Arg Glu Ser His Gln Ile Gly Asp
 115 120 125
 Ala Tyr Ser Asn Ser Asp Lys Ser Leu Thr Glu Leu Glu Ser Lys Phe
 130 135 140
 Lys Gln Gly Gln Glu Gln Asp Ser Arg Gln Glu Ser Arg Leu Asn Glu
 145 150 155 160
 Asp Phe Leu Gly Met Leu Val His Thr Arg Ser Leu Leu Lys Glu Thr
 165 170 175
 Leu Asp Ile Ser Val Gly Leu Arg Asp Lys Tyr Glu Leu Leu Ala Leu
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 Thr Ile Arg Ser His Gly Thr Arg Leu Gly Arg Leu Lys Asn Asp Tyr
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<210> 13
 <211> 2020
 <212> DNA
 <213> Homo sapiens

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11.

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 <213> Homo sapiens

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 35 40 45
 Phe Asn Leu Pro Val Lys Gln Trp Tyr Phe Asn Ser Ser Asp Asn Asn
 50 55 60
 Leu Gln Tyr Trp Gly Leu Asp Tyr Pro Pro Leu Thr Ala Tyr His Ser
 65 70 75 80
 Leu Leu Cys Ala Tyr Val Ala Lys Phe Ile Asn Pro Asp Trp Ile Ala
 85 90 95
 Leu His Thr Ser Arg Gly Tyr Glu Ser Gln Ala His Lys Leu Phe Met
 100 105 110
 Arg Thr Thr Val Leu Ile Ala Asp Leu Leu Ile Tyr Ile Pro Ala Val
 115 120 125
 Val Leu Tyr Cys Cys Cys Leu Lys Glu Ile Ser Thr Lys Lys Lys Ile
 130 135 140
 Ala Asn Ala Leu Cys Ile Leu Leu Tyr Pro Gly Leu Ile Leu Ile Asp
 145 150 155 160
 Tyr Gly His Phe Gln Tyr Asn Ser Val Ser Leu Gly Phe Ala Leu Trp
 165 170 175
 Gly Val Leu Gly Ile Ser Cys Asp Cys Asp Leu Leu Gly Ser Leu Ala
 180 185 190
 Phe Cys Leu Ala Ile Asn Tyr Lys Gln Met Glu Leu Tyr His Ala Leu
 195 200 205
 Pro Phe Phe Cys Phe Leu Leu Gly Lys Cys Phe Lys Lys Gly Leu Lys
 210 215 220
 Gly Lys Gly Phe Val Xaa Leu Val Lys Leu Ala Xaa Ile Val Val Ala
 225 230 235 240
 Ser Phe Val Leu Cys Trp Leu Pro Phe Phe Thr Glu Arg Glu Gln Thr
 245 250 255
 Leu Gln Val Leu Arg Arg Leu Phe Pro Val Asp Arg Gly Leu Phe Glu
 260 265 270
 Asp Lys Val Ala Asn Ile Trp Cys Ser Phe Asn Val Phe Leu Lys Ile
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 305 310 315 320
 Ser Ser Lys Gly Phe Lys Phe Thr Leu Val Ser Cys Ala Leu Ser Phe
 325 330 335
 Phe Leu Phe Ser Phe Gln Val His Glu Lys Ser Ile Leu Leu Val Ser
 340 345 350
 Leu Pro Val Cys Leu Val Leu Ser Glu Ile Pro Phe Met Ser Thr Trp
 355 360 365

Phe Leu Leu Val Ser Thr Phe Ser Met Leu Pro Leu Leu Leu Lys Asp
 370 375 380
 Glu Leu Leu Met Pro Ser Val Val Thr Thr Met Ala Phe Phe Ile Ala
 385 390 395 400
 Cys Val Thr Ser Phe Ser Ile Phe Glu Lys Thr Ser Glu Glu Glu Leu
 405 410 415
 Gln Leu Lys Ser Phe Ser Ile Ser Val Arg Lys Tyr Leu Pro Cys Xaa
 420 425 430
 Thr Phe Leu Ser Arg Ile Xaa Gln Tyr Leu Phe Leu Ile Ser Val Ile
 435 440 445
 Thr Met Val Leu Leu Thr Leu Met Thr Val Thr Leu Asp Pro Pro Gln
 450 455 460
 Lys Leu Pro Asp Leu Phe Ser Val Leu Val Cys Xaa Val Ser Cys Leu
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 Asn Phe Leu Phe Phe Leu Val Tyr Phe Asn Ile Ile Ile Met Trp Asp
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<210> 15
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 <213> Homo sapiens

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<210> 16
 <211> 130
 <212> PRT
 <213> Homo sapiens

<400> 16
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20 25 30

Lys Thr Pro Val Ile Gln Leu Val Leu Phe Ile Ile Gln Asp Ile Ala
35 40 45

Val Leu Phe Asn Ile Ile Ile Ile Phe Leu Met Phe Phe Asn Thr Phe
50 55 60

Val Phe Gln Ala Gly Leu Val Asn Leu Leu Phe His Lys Phe Lys Gly
65 70 75 80

Thr Ile Ile Leu Thr Ala Val Tyr Phe Ala Leu Ser Ile Ser Leu His
85 90 95

Val Trp Val Met Asn Leu Arg Trp Lys Asn Ser Asn Ser Phe Ile Trp
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Glu Phe
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<212> DNA
<213> Homo sapiens
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<210> 18
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<212> PRT
<213> Homo sapiens
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<400> 18

15.

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 20 25 30
 Leu Leu Ala Gln Lys Val Met Tyr Leu Leu Val Pro Leu Leu Asn Arg
 35 40 45
 Gly Asn Asp Lys His Lys Leu Thr Ser Ala Gly Phe Phe Val Glu Leu
 50 55 60
 Leu Arg Ser Pro Val Ala Lys Arg Leu Pro Ser Ile Tyr Ser Val Ala
 65 70 75 80
 Arg Phe Lys Asp Trp Leu Gln Asp Gly Asn His Leu Phe Arg Ile Leu
 85 90 95
 Gly Leu Arg Gly Leu Tyr Asn Leu Val Gly His Gln Glu Met Arg Glu
 100 105 110
 Asp Ile Lys Ser Leu Leu Pro Tyr Ile Val Asp Ser Leu Arg Glu Thr
 115 120 125
 Asp Glu Lys Ile Val Leu Ser Ala Ile Gln Ile Leu Leu Gln Leu Val
 130 135 140
 Arg Thr Met Asp Phe Thr Thr Leu Ala Ala Met Met Arg Thr Leu Phe
 145 150 155 160
 Ser Leu Phe Gly Asp Val Arg Ser Asp Val His Arg Phe Ser Val Thr
 165 170 175
 Leu Phe Gly Ala Ala Ile Lys Ser Val Lys Asn Pro Asp Lys Lys Ser
 180 185 190
 Ile Glu Asn Gln Val Leu Asp Ser Leu Val Pro Leu Leu Leu Tyr Ser
 195 200 205
 Gln Asp Glu Asn Asp Ala Val Ala Glu Glu Ser Arg Gln Val Leu Thr
 210 215 220
 Ile Cys Ala Gln Phe Leu Lys Trp Lys Leu Pro Gln Glu Val Tyr Ser
 225 230 235 240
 Lys Asp Pro Trp His Ile Lys Pro Thr Glu Ala Gly Thr Ile Cys Arg
 245 250 255
 Phe Phe Glu Lys Lys Cys Lys Gly Lys Ile Asn Ile Leu Glu Gln Thr
 260 265 270
 Leu Met Tyr Ser Lys Asn Pro Lys Leu Pro Ile Arg Arg Ser Ala Val
 275 280 285
 Leu Phe Val Gly Leu Leu Ser Lys Tyr Met Asp His Asn Glu Leu Arg
 290 295 300
 Arg Met Gly Thr Asp Trp Ile Glu Asp Asp Leu Arg Asp Leu Leu Cys
 305 310 315 320
 Asp Pro Glu Pro Ser Leu Cys Ile Ile Ala Ser Gln Thr Leu Leu Leu
 325 330 335

Val Gln Met Ala Arg Ala Glu Pro Lys Pro Lys Gln Arg Val Asn Trp
 340 345 350

Leu Gln Lys Leu Met Gly Arg Ser Ser Ala
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<210> 19
 <211> 1656
 <212> DNA
 <213> Homo sapiens

<400> 19
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 <212> PRT
 <213> Homo sapiens

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 35 40 45
 His Asp Leu Ile Phe Trp Arg Asp Val Lys Lys Thr Gly Phe Val Phe
 50 55 60

17

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 Phe Arg Ile Tyr Lys Ser Val Ile Gln Ala Val Gln Lys Ser Glu Glu
 100 105 110
 Gly His Pro Phe Lys Ala Tyr Leu Asp Val Asp Ile Thr Leu Ser Ser
 115 120 125
 Glu Ala Phe His Asn Tyr Met Asn Ala Ala Met Val His Ile Asn Arg
 130 135 140
 Ala Leu Lys Leu Ile Ile Arg Leu Phe Leu Val Glu Asp Leu Val Asp
 145 150 155 160
 Ser Leu Lys Leu Ala Val Phe Met Trp Leu Met Thr Tyr Val Gly Ala
 165 170 175
 Val Phe Asn Gly Ile Thr Leu Leu Ile Leu Ala Glu Leu Leu Ile Phe
 180 185 190
 Ser Val Pro Ile Val Tyr Glu Lys Tyr Lys Thr Gln Ile Asp His Tyr
 195 200 205
 Val Gly Ile Ala Arg Asp Gln Thr Lys Ser Ile Val Glu Lys Ile Gln
 210 215 220
 Ala Lys Leu Pro Gly Ile Ala Lys Lys Lys Ala Glu
 225 230 235

<210> 21
 <211> 2439
 <212> DNA
 <213> Homo sapiens

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<210> 22

<211> 47

<212> PRT

<213> Homo sapiens

<400> 22

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      20             25             30

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Ser Phe Cys Val Ser Asn Asn Lys Asp His Ile Phe Leu Val Asn
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<210> 23

<211> 1132

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (1009)

<400> 23

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tatacacaca caatttccca gttcgtattt ttcattatgt catgtacctt attgatagct 960

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19

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<210> 24
 <211> 98
 <212> PRT
 <213> Homo sapiens

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 20 25 30
 Met Tyr Phe Ser Pro Leu Tyr Phe Ile Ile Phe Leu Lys Ser Ser Asn
 35 40 45
 Leu Asn Thr Trp Thr Ser Tyr Trp Ile Thr Leu Ile His Ile Phe Ile
 50 55 60
 Ile Leu Ser Ile His Phe Ala Thr Tyr Thr Pro Cys Asp Asp Phe Lys
 65 70 75 80
 Pro Asp Phe Cys Ile Glu Asn Val Lys Arg Met Ala Phe Phe Arg Gly
 85 90 95

Ser Lys

<210> 25
 <211> 401
 <212> DNA
 <213> Homo sapiens

<400> 25
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 gtggctaaat aaccaaacat ttgtgtaaaa aaaaaaaaaa a 401

<210> 26
 <211> 38
 <212> PRT
 <213> Homo sapiens

<400> 26
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 Met Phe Glu Ile Gln Glu
 35

<210> 27
 <211> 755
 <212> DNA
 <213> Homo sapiens

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<210> 28
 <211> 86
 <212> PRT
 <213> Homo sapiens

<400> 28
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 20 25 30
 Lys Phe Leu Glu Val Arg Phe Pro Gly Gln Arg Leu Asn Ala His Val
 35 40 45
 Ile Leu Leu Asp Ile Val Lys Ser Pro Tyr Arg Ala Cys Thr Thr Gln
 50 55 60
 His Ser Pro Gln Arg Cys Met Arg Gly Thr Ile Ser Pro Trp Pro His
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<210> 29
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 <212> DNA
 <213> Homo sapiens

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21

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<210> 30
 <211> 186
 <212> PRT
 <213> Homo sapiens

<400> 30
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 35 40 45
 Gly Ser Ser Val Thr Ser Ser Gly Val Ser Thr Ala Thr Ile Ser Gly
 50 55 60
 Ser Ser Val Thr Ser Asn Gly Val Ser Ile Val Thr Asn Ser Glu Phe
 65 70 75 80
 His Thr Thr Ser Ser Gly Ile Ser Thr Ala Thr Asn Ser Glu Phe Ser
 85 90 95
 Thr Ala Ser Ser Gly Ile Ser Ile Ala Thr Asn Ser Glu Ser Ser Thr
 100 105 110
 Thr Ser Ser Gly Ala Ser Thr Ala Thr Asn Ser Glu Ser Ser Thr Pro
 115 120 125
 Ser Ser Gly Ala Ser Thr Ala Thr Asn Ser Asp Ser Ser Thr Thr Ser
 130 135 140
 Ser Gly Ala Ser Thr Ala Thr Asn Ser Asp Ser Ser Leu Gly Asn Lys
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<210> 31
 <211> 3285
 <212> DNA
 <213> Homo sapiens

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<210> 32

<211> 184

<212> PRT

<213> Homo sapiens

<400> 32

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Met Ile Ser Phe Ala Val Gln Lys Leu Phe Ser Ser Met Gln Ser Cys
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Met Phe Ile Phe Leu Leu Leu Leu Val Leu Leu Gly Ser Tyr Ala Arg
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Ser Asp Thr Thr Leu Lys Pro Arg Pro Val Ser Trp Ser Phe Ser Pro
  35             40             45

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Val Phe Ser Ser Thr Gly Phe Thr Val Ser Gly Leu Thr Ile Lys Pro
50 55 60

Leu Ser Ile Leu Asn Gly Phe Leu Cys Arg Asp Ile Pro Ser Thr Arg
65 70 75 80

Ala Ser Ser Gly Leu Ala Asp Ala Pro Pro Ser Pro Leu Cys Pro Leu
85 90 95

His Ser Thr Leu Phe Met Trp Lys Asn Pro Trp His Pro Arg Val Ala
100 105 110

Ser Leu Ser Tyr Pro Ala Pro His Gly Asp Leu Thr Leu Ala Ser Leu
115 120 125

Thr Trp Val Ser Leu Pro Asn Pro Leu Pro Gly Pro Thr Thr Ala Ser
130 135 140

Ile Pro Asp Leu Pro Arg Gly Pro Ile Pro Ala Val Leu Arg His Leu
145 150 155 160

Arg Ala Val Ser Glu Leu Phe Ser Leu Thr Val His Asn Arg Ser Ala
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Lys Glu Ser Cys Arg Leu Phe Leu
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<210> 33

<211> 1819

<212> DNA

<213> Homo sapiens

<400> 33

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24.

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 <213> Homo sapiens

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 20 25 30
 Arg Ile Lys Ala Pro Ser Gly Gln Ser Ile Arg Asn Thr Glu Asn Lys
 35 40 45
 Glu Asn Ile Val Asn Thr Arg Phe Glu Gly Ile Lys Cys Leu Tyr Ile
 50 55 60
 Leu Tyr Lys Cys Lys His Gly Leu Val Thr Lys
 65 70 75

<210> 35
 <211> 1269
 <212> DNA
 <213> Homo sapiens

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 aaaaaaaaaa 1269

<210> 36
 <211> 100
 <212> PRT
 <213> Homo sapiens

<400> 36

25

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 Val Ile Ile Val Phe Trp Glu Phe Ile Asn Ser Thr Glu Gly Ser Phe
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 Leu Trp Ile Tyr His Ser Lys Asn Pro Glu Val Asp Asp Ser Ser Ala
 35 40 45
 Gln Lys Gly Trp Trp Phe Leu Ser Trp Phe Asn Asn Gly Ile His Asn
 50 55 60
 Tyr Gln Gln Gly Glu Glu Asp Ile Asp Lys Glu Lys Gly Arg Glu Glu
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 Thr Lys Gly Arg Lys Met Thr Gln Gln Ser Phe Gly Tyr Gly Thr Gly
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 Leu Ile Gln Thr
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 <211> 232
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 <213> Homo sapiens

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<210> 38
 <211> 57
 <212> PRT
 <213> Homo sapiens

<400> 38
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<210> 39
 <211> 1135
 <212> DNA
 <213> Homo sapiens

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<210> 40

<211> 54

<212> PRT

<213> Homo sapiens

<400> 40

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Met Lys Phe Gln Leu Leu Asn Leu Leu Pro Tyr Pro Gly Leu Trp Thr
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Gln Thr Gly Leu Glu Pro Gln Ser Leu Phe Pro Ser Ser Pro Ser Ser
      20             25             30

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Pro Cys Gly Leu Pro Gly Leu Ser Ile Cys Tyr Cys Ala Val Leu Gly
   35             40             45

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Ile Gly Ala Glu Val Ala
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<210> 41

<211> 4292

<212> DNA

<213> Homo sapiens

<400> 41

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<210> 42

<211> 1369

<212> PRT

<213> Homo sapiens

<400> 42

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 Asp Tyr Arg Gly Pro Asp Cys Arg Tyr Leu Asn Phe Thr Lys Gly Glu
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 Glu Ile Ser Val Tyr Val Lys Leu Ala Gly Glu Arg Glu Asp Leu Trp
 65 70 75 80
 Ala Gly Ser Lys Gly Lys Glu Phe Gly Tyr Phe Pro Arg Asp Ala Val
 85 90 95
 Gln Ile Glu Glu Val Phe Ile Ser Glu Glu Ile Gln Met Ser Thr Lys
 100 105 110
 Glu Ser Asp Phe Leu Cys Leu Leu Gly Val Ser Tyr Thr Phe Asp Asn
 115 120 125
 Glu Asp Ser Glu Leu Asn Gly Asp Tyr Gly Glu Asn Ile Tyr Pro Tyr
 130 135 140
 Glu Glu Asp Lys Asp Glu Lys Ser Ser Ile Tyr Glu Ser Asp Phe Gln
 145 150 155 160
 Ile Glu Pro Gly Phe Tyr Ala Thr Tyr Glu Ser Thr Leu Phe Glu Asp
 165 170 175
 Gln Val Pro Ala Leu Glu Ala Pro Glu Asp Ile Gly Ser Thr Ser Glu
 180 185 190
 Ser Lys Asp Trp Glu Glu Val Val Val Glu Ser Met Glu Gln Asp Arg
 195 200 205
 Ile Pro Glu Val His Val Pro Pro Ser Ser Ala Val Ser Gly Val Lys
 210 215 220
 Glu Trp Phe Gly Leu Gly Gly Glu Gln Ala Glu Glu Lys Ala Phe Glu
 225 230 235 240
 Ser Val Ile Glu Pro Val Gln Glu Ser Ser Phe Arg Ser Arg Lys Ile
 245 250 255
 Ala Val Glu Asp Glu Asn Asp Leu Glu Glu Leu Asn Asn Gly Glu Pro
 260 265 270
 Gln Thr Glu His Gln Gln Glu Ser Glu Ser Glu Ile Asp Ser Val Pro
 275 280 285
 Lys Thr Gln Ser Glu Leu Ala Ser Glu Ser Glu His Ile Pro Lys Pro
 290 295 300
 Gln Ser Thr Gly Trp Phe Gly Gly Gly Phe Thr Ser Tyr Leu Gly Phe
 305 310 315 320
 Gly Asp Glu Asp Thr Gly Leu Glu Leu Ile Ala Glu Glu Ser Asn Pro
 325 330 335
 Pro Leu Gln Asp Phe Pro Asn Pro Ile Ser Ser Asp Lys Glu Ala Thr
 340 345 350

29.

Val Pro Cys Thr Glu Ile Leu Thr Glu Lys Lys Asp Thr Ile Thr Asn
 355 360 365
 Asp Ser Leu Ser Leu Lys Pro Ser Trp Phe Asp Phe Gly Phe Ala Ile
 370 375 380
 Leu Gly Phe Ala Tyr Ala Lys Glu Asp Lys Ile Met Leu Asp Asp Arg
 385 390 395 400
 Lys Asn Glu Glu Asp Gly Gly Ala Asp Glu His Glu His Pro Leu Thr
 405 410 415
 Ser Glu Leu Asp Pro Glu Lys Glu Gln Glu Ile Glu Thr Ile Lys Ile
 420 425 430
 Ile Glu Thr Glu Asp Gln Ile Asp Lys Lys Pro Val Ser Glu Lys Thr
 435 440 445
 Asp Glu Ser Asp Thr Ile Pro Tyr Leu Lys Lys Phe Leu Tyr Asn Phe
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 Asp Asn Pro Trp Asn Phe Gln Asn Ile Pro Lys Glu Thr Glu Leu Pro
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 Phe Pro Lys Gln Ile Leu Asp Gln Asn Asn Val Ile Glu Asn Glu Glu
 485 490 495
 Thr Gly Glu Phe Ser Ile Asp Asn Tyr Pro Thr Asp Asn Thr Lys Val
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 Met Ile Phe Lys Ser Ser Tyr Ser Leu Ser Asp Met Val Ser Asn Ile
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 Glu Leu Pro Thr Arg Ile His Glu Glu Val Tyr Phe Glu Pro Ser Ser
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 Ser Lys Asp Ser Asp Glu Asn Ser Lys Pro Ser Val Asp Thr Glu Gly
 545 550 555 560
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 580 585 590
 Ser Gln Lys Glu Asp Ala Ser Glu Phe Gln Ile Leu Lys Tyr Leu Phe
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 Gln Ile Asp Val Tyr Asp Phe Met Asn Ser Ala Phe Ser Pro Ile Val
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 Ile Leu Thr Glu Arg Val Val Ala Ala Leu Pro Glu Gly Met Arg Pro
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 Asp Ser Asn Leu Tyr Gly Phe Pro Trp Glu Leu Val Ile Cys Ala Ala
 645 650 655
 Val Val Gly Phe Phe Ala Val Leu Phe Phe Leu Trp Arg Ser Phe Arg
 660 665 670

30.

Ser Val Arg Ser Arg Leu Tyr Val Gly Arg Glu Lys Lys Leu Ala Leu
 675 680 685
 Met Leu Ser Gly Leu Ile Glu Glu Lys Ser Lys Leu Leu Glu Lys Phe
 690 695 700
 Ser Leu Val Gln Lys Glu Tyr Glu Gly Tyr Glu Val Glu Ser Ser Leu
 705 710 715 720
 Lys Asp Ala Ser Phe Glu Lys Glu Ala Thr Glu Ala Gln Ser Leu Glu
 725 730 735
 Ala Thr Cys Glu Lys Leu Asn Arg Ser Asn Ser Glu Leu Glu Asp Glu
 740 745 750
 Ile Leu Cys Leu Glu Lys Glu Leu Lys Glu Glu Lys Ser Lys His Ser
 755 760 765
 Glu Gln Asp Glu Leu Met Ala Asp Ile Ser Lys Arg Ile Gln Ser Leu
 770 775 780
 Glu Asp Glu Ser Lys Ser Leu Lys Ser Gln Val Ala Glu Ala Lys Met
 785 790 795 800
 Thr Phe Lys Ile Phe Gln Met Asn Glu Glu Arg Leu Lys Ile Ala Ile
 805 810 815
 Lys Asp Ala Leu Asn Glu Asn Ser Gln Leu Gln Glu Ser Gln Lys Gln
 820 825 830
 Leu Leu Gln Glu Ala Glu Val Trp Lys Glu Gln Val Ser Glu Leu Asn
 835 840 845
 Lys Gln Lys Val Thr Phe Glu Asp Ser Lys Val His Ala Glu Gln Val
 850 855 860
 Leu Asn Asp Lys Glu Ser His Ile Lys Thr Leu Thr Glu Arg Leu Leu
 865 870 875 880
 Lys Met Lys Asp Trp Ala Ala Met Leu Gly Glu Asp Ile Thr Asp Asp
 885 890 895
 Asp Asn Leu Glu Leu Glu Met Asn Ser Glu Ser Glu Asn Gly Ala Tyr
 900 905 910
 Leu Asp Asn Pro Pro Lys Gly Ala Leu Lys Lys Leu Ile His Ala Ala
 915 920 925
 Lys Leu Asn Ala Ser Leu Lys Thr Leu Glu Gly Glu Arg Asn Gln Ile
 930 935 940
 Tyr Ile Gln Leu Ser Glu Val Asp Lys Thr Lys Glu Glu Leu Thr Glu
 945 950 955 960
 His Ile Lys Asn Leu Gln Thr Gln Gln Ala Ser Leu Gln Ser Glu Asn
 965 970 975
 Thr His Phe Glu Asn Glu Asn Gln Lys Leu Gln Gln Lys Leu Lys Val
 980 985 990
 Met Thr Glu Leu Tyr Gln Glu Asn Glu Met Lys Leu His Arg Lys Leu
 995 1000 1005

Thr Val Glu Glu Asn Tyr Arg Leu Glu Lys Glu Glu Lys Leu Ser Lys
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 Val Asp Glu Lys Ile Ser His Ala Thr Glu Glu Leu Glu Thr Tyr Arg
 1025 1030 1035 1040
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 1045 1050 1055
 Tyr Gln Gly Gln Ile Ile Ser His Glu Lys Lys Ala His Asp Asn Trp
 1060 1065 1070
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 1075 1080 1085
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 1090 1095 1100
 Leu Leu Glu Lys Asp Pro Tyr Ala Leu Asp Val Pro Asn Thr Ala Phe
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 1125 1130 1135
 Asn Glu Arg Gly Glu Ser Ser Cys Asp Arg Leu Thr Asp Pro His Arg
 1140 1145 1150
 Ala Pro Ser Asp Thr Gly Ser Leu Ser Pro Pro Trp Asp Gln Asp Arg
 1155 1160 1165
 Arg Met Met Phe Pro Pro Gly Gln Ser Tyr Pro Asp Ser Ala Leu
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 Pro Pro Gln Arg Gln Asp Arg Phe Cys Ser Asn Ser Gly Arg Leu Ser
 1185 1190 1195 1200
 Gly Pro Ala Glu Leu Arg Ser Phe Asn Met Pro Ser Leu Asp Lys Met
 1205 1210 1215
 Asp Gly Ser Met Pro Ser Glu Met Glu Ser Ser Arg Asn Asp Thr Lys
 1220 1225 1230
 Asp Asp Leu Gly Asn Leu Asn Val Pro Asp Ser Ser Leu Pro Ala Glu
 1235 1240 1245
 Asn Glu Ala Thr Gly Pro Gly Phe Val Pro Pro Pro Leu Ala Pro Ile
 1250 1255 1260
 Arg Gly Pro Leu Phe Pro Val Asp Ala Arg Gly Pro Phe Leu Arg Arg
 1265 1270 1275 1280
 Gly Pro Pro Phe Pro Pro Pro Pro Pro Gly Ala Met Phe Gly Ala Ser
 1285 1290 1295
 Arg Asp Tyr Phe Pro Pro Arg Asp Phe Pro Gly Pro Pro Pro Ala Pro
 1300 1305 1310
 Phe Ala Met Arg Asn Val Tyr Pro Pro Arg Gly Phe Pro Pro Tyr Leu
 1315 1320 1325

32,

Pro Pro Arg Pro Gly Phe Phe Pro Pro Pro Pro His Ser Glu Gly Arg
1330 1335 1340

Ser Glu Phe Pro Ser Gly Leu Ile Pro Pro Ser Asn Glu Pro Ala Thr
1345 1350 1355 1360

Glu His Pro Glu Pro Gln Gln Glu Thr
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<210> 43
<211> 412
<212> DNA
<213> Homo sapiens

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gcactccagc ctgggcgaca gagcgagacc ccatctcaaa aaaaaaaaaa aa 412

<210> 44
<211> 49
<212> PRT
<213> Homo sapiens

<400> 44
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Arg Pro Gly Pro Val Pro Ser Cys Ser Leu Val Leu Leu Thr Pro Leu
20 25 30

Ala Pro Leu Pro Leu Thr Ala Arg Glu Ser Leu Cys Pro Cys Pro Pro
35 40 45

Ser

<210> 45
<211> 1317
<212> DNA
<213> Homo sapiens

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aagccatgtg taacagagct tagacatcca aaactaatca atgctgaggt ggctaaatac 180
ctagcctttt acatgtaaac ctgtctgcaa aattagcttt tttaaaaaaaa aaaaaaaaaa 240
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acgtggttgt gggaggggaa agaggaaaca gagctagtca gatgtgaatt gtatctgttg 780

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<210> 46

<211> 48

<212> PRT

<213> Homo sapiens

<400> 46

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Met Phe Phe Ile Ser Arg Val Phe Pro Phe Pro Ser Glu Ile Leu Ile
  1             5             10             15

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Leu Ser Ile Phe Leu Arg Leu Leu Phe Ile Ser Phe Leu Lys Ala Leu
      20             25             30

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Leu Leu Trp His Phe Ser Ile Thr Phe Ser Phe Leu Cys Thr Val Ala
  35             40             45

```

<210> 47

<211> 1442

<212> DNA

<213> Homo sapiens

<400> 47

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1442

<210> 48

<211> 247

<212> PRT

<213> Homo sapiens

<400> 48

Met Leu Arg Phe Ile Gln Lys Phe Ser Gln Ala Ser Ser Lys Ile Leu
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Lys Tyr Ser Phe Pro Val Gly Leu Arg Thr Ser Arg Thr Asp Ile Leu
 20 25 30

Ser Leu Lys Met Ser Leu Gln Gln Asn Phe Ser Pro Cys Pro Arg Pro
 35 40 45

Trp Leu Ser Ser Ser Phe Pro Ala Tyr Met Ser Lys Thr Gln Cys Tyr
 50 55 60

His Thr Ser Pro Cys Ser Phe Lys Lys Gln Gln Lys Gln Ala Leu Leu
 65 70 75 80

Ala Arg Pro Ser Ser Thr Ile Thr Tyr Leu Thr Asp Ser Pro Lys Pro
 85 90 95

Ala Leu Cys Val Thr Leu Ala Gly Leu Ile Pro Phe Val Ala Pro Pro
 100 105 110

Leu Val Met Leu Met Thr Lys Thr Tyr Ile Pro Ile Leu Ala Phe Thr
 115 120 125

Gln Met Ala Tyr Gly Ala Ser Phe Leu Ser Phe Leu Gly Gly Ile Arg
 130 135 140

Trp Gly Phe Ala Leu Pro Glu Gly Ser Pro Ala Lys Pro Asp Tyr Leu
 145 150 155 160

Asn Leu Ala Ser Ser Ala Ala Pro Leu Phe Phe Ser Trp Phe Ala Phe
 165 170 175

Leu Ile Ser Glu Arg Leu Ser Glu Ala Ile Val Thr Val Ile Met Gly
 180 185 190

Met Gly Val Ala Phe His Leu Glu Leu Phe Leu Leu Pro His Tyr Pro
 195 200 205

Asn Trp Phe Lys Ala Leu Arg Ile Val Val Thr Leu Leu Ala Thr Phe
 210 215 220

Ser Phe Ile Ile Thr Leu Val Val Lys Ser Ser Phe Pro Glu Lys Gly
 225 230 235 240

His Lys Arg Pro Gly Gln Val
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<210> 49

<211> 2696

<212> DNA

<213> Homo sapiens

<400> 49

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35,

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gctgaagcat gtacttcctg tattggacag tgaccagtct ctgacctgcc ttctccctcc 480
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<210> 50

<211> 73

<212> PRT

<213> Homo sapiens

<400> 50

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Met Asn Ser Phe Ala Tyr His Ser His Pro Pro Leu Gly Ser Arg Phe
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Leu Gln Thr His Ser Leu Glu Ser Gly Ser Gln Ser Ala Gly Ser Arg
  20                      25                      30

```

```

Thr Pro Leu Thr Gln Thr His Leu Arg Arg Leu Gly Leu Leu Lys Ser
  35                      40                      45

```

```

Val Cys Leu Gly Cys Leu Cys Asn Asn Pro Ser Leu Phe Ile Phe Leu
  50                      55                      60

```

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Gly Asp Pro Leu Pro Ser Gln Pro Gly
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<210> 51
<211> 2791
<212> DNA
<213> Homo sapiens

<400> 51

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<210> 52
<211> 219
<212> PRT
<213> Homo sapiens

<400> 52

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Leu Met Leu Pro Val Leu Ser Ala Thr Leu Gln Val Arg Thr Ser Cys
 20 25 30

Pro Ser Phe Val Leu Val Thr Arg Pro Val Ser Ser Thr Met Lys Ile
 35 40 45

Arg Phe Arg Phe Leu Ser Pro Gly Leu Ile Ser Phe Thr Lys Val Ser
 50 55 60

Val Val Met Leu Pro Glu Pro Arg His Pro Thr Gly Trp Gly Ile Glu
 65 70 75 80

Asp Glu Gly Ser Met Leu Gly Ser Phe Ala Pro Met Leu His Phe Pro
 85 90 95

Arg Pro Thr Tyr Pro Ile Arg Met Gly Ser Gly Ser Leu Asn Pro Ser
 100 105 110

Asn Pro Ser Lys Arg Leu Lys Lys Asn Ile Pro Gly Gly Leu Gln Leu
 115 120 125

Gln Asp Gln Asn Leu Gly Val Ser Gly Gln Ala Ala Leu Gly Leu Glu
 130 135 140

Gly Pro Leu Pro Gly Cys Ser Phe Ser Leu Lys Pro Arg Ser Gly Gly
 145 150 155 160

Ala Asp Val Asp Arg Gly Arg Glu Pro Gly Ala Gln Pro Gly Ser Arg
 165 170 175

Ile Leu Leu Ala Arg Ser Ser Gly Thr Leu Ile Pro Thr Ser Arg Asp
 180 185 190

Ser Val His Pro Leu Pro Tyr Arg Gln Pro Thr Thr His Pro Ser Gln
 195 200 205

Pro Ala Gly Leu Cys Arg Gly Trp Lys Leu Leu
 210 215

<210> 53

<211> 1527

<212> DNA

<213> Homo sapiens

<400> 53

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 tttagtaaac ctgaactatg ctgtgctgct gtacaaccag ggcgagaaga agaacgccct 240
 ggcccaatat caggagatgg agaagaaagt cagcctactc aaggacaata gctctctgga 300
 atttgactct gagatgggtg agatggctca gaagttggga gctgctctcc aggttgggga 360
 ggactgggtc tggaccaaac cagttaaaga tcccaaatca aagcaccaga ccacttcaac 420
 cagcaaacct gccagtttcc agcagcctct gggctctaata caagctctag gacaggcaat 480
 gtcttcagca gctgcataca ggacgctccc ctcagggtgct ggaggaacat cccagttcac 540
 aaagccccca tctcttcttc tggagccaga gcctgcggtg gaatcaagtc caactgaaac 600
 atcagaacaa ataagagaga aataagaata gaatgaatga ccccaaaata gggttttctt 660
 gggcgaggat gtgctggatt aggaaagggtg acatgacaca ggcagagcag agtggcacc 720

```

accacagaat acagtgtgtg ttattacgag gagccagcag ttgagcctaa ggtccttcta 780
cctacctggt attggcattt gaggtcggaa accctctact gcccataag ccaggaaaag 840
tgaaaagaga acacagttcc tttaagaact ggcagcaagg cttgaggcct tatgtatgta 900
gctgagtcag caaggtacat gatgctgtct gctttcaaaa ggacttttct ctctagctg 960
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atgacaaagc cttggtttaa ctgagggtgat cctcagggtg tgaggtttat tagtcccaa 1080
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aacaaaagcc ctggaagttg aggccaagcc tgctgagtat tgcagctgca ttgcccataa 1200
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agatcctatc aggatgagga gcagcagccc agggcttgtc tggatmagca ccaacgattt 1320
taaagaaaaa aggaagagtt tcttagatga gtaattgtta ttgaagatag tcagtataa 1380
ccactgacca gatgctatca atacastatg tgtccttttt agaataaaga ttacatatca 1440
tcatttcctt tggggaaaat tgttattcag gtataaaaac aagagatcat aataaaaacc 1500
taaaagaacc taaaaaaaaa aaaaaaa 1527

```

<210> 54

<211> 122

<212> PRT

<213> Homo sapiens

<400> 54

```

Met Glu Lys Lys Val Ser Leu Leu Lys Asp Asn Ser Ser Leu Glu Phe
  1                      5                      10                      15

```

```

Asp Ser Glu Met Val Glu Met Ala Gln Lys Leu Gly Ala Ala Leu Gln
      20                      25                      30

```

```

Val Gly Glu Ala Leu Val Trp Thr Lys Pro Val Lys Asp Pro Lys Ser
    35                      40                      45

```

```

Lys His Gln Thr Thr Ser Thr Ser Lys Pro Ala Ser Phe Gln Gln Pro
    50                      55                      60

```

```

Leu Gly Ser Asn Gln Ala Leu Gly Gln Ala Met Ser Ser Ala Ala Ala
    65                      70                      75                      80

```

```

Tyr Arg Thr Leu Pro Ser Gly Ala Gly Gly Thr Ser Gln Phe Thr Lys
      85                      90                      95

```

```

Pro Pro Ser Leu Pro Leu Glu Pro Glu Pro Ala Val Glu Ser Ser Pro
    100                      105                      110

```

```

Thr Glu Thr Ser Glu Gln Ile Arg Glu Lys
    115                      120

```

<210> 55

<211> 2352

<212> DNA

<213> Homo sapiens

<400> 55

```

agcagagtga gctgaagctc ctgaggaggg ttcccgaagg ggggcgctca gagatggggg 60
cagggggcgg ggagaggaga gtctgcctta tgtcccttcc ttgtggactt cacatgggtca 120
tgcaggaaagt gaggatgggt gtccagcggg ggccgaggcc actagtatcc tcctgcttcc 180
cctgccatt ctccagggct ggactgaccc tatggactgg gagagagtgc ctgaggccac 240
catgccacag tcaaaggggg tcctatctca gaagggtggca gcatccactg agatatcctc 300
acccgaaggg aaggaggctg ctgggtagca aataagcccc ttcttttctt ggtgagttga 360
tgacctccaa tagctcccag tgtcatgggt acccagtagc cattagctgg tgttgggttg 420
attgagacct ggggcagttc ctggggcagg aagccagatg ggagatgaga tagaaagtgt 480
taggagttat cctctttgcc tggcctttga gaataactta ctgtgtgact ttgggcaagt 540
tccttcccca ctctgggcct cagtttctca cttgggaaag caaggagttt gaccagatga 600

```

```

tcacaatggg ccttcctagc tctggccacc aagaatttgt gaacattaga gctcctgggc 660
tggtagggtag agccagagct gctgactggt ctctctgcct ccagagggga tttattggac 720
ctcagagggtg gcagggccct atggagcacc aactgccctc aacccacccc tgtgcccagg 780
actgggaagg gattgatgtc aggctgtggc cataggtagc atgagttgcc caaggaggga 840
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cagccccctg tgggcacaga caccctgagg tttacccagg caaatatatt gattagcagg 960
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tggctgctgg tccctatggt gccttgatgt gaattagaag acggtgccct ttccagggtg 1860
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ctggtacagt tttatgcttt gtggtgtggc ttttaatttt tataaacatg tcttactgct 2280
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aaaaaaaaaa aa                                     2352

```

<210> 56

<211> 169

<212> PRT

<213> Homo sapiens

<400> 56

```

Met Lys Cys Trp Ser Asn Ala Trp Gln Thr Tyr Ala Leu Gln Cys Leu
  1             5             10             15

```

```

Leu Lys Pro Leu Gly Leu Thr Gln Asp Pro Leu Val Phe Gly Met Thr
      20             25             30

```

```

Ser Phe Leu Gln Thr Ser Ser Pro Ile Pro Asn Ser Cys Met Glu Asn
  35             40             45

```

```

Val Cys Gln Ala Gly Phe Pro Ser Leu Leu His Leu Asn Ile Thr Leu
  50             55             60

```

```

Thr Leu Leu Gly Leu Ala Gln Cys Tyr Leu Ala Asn Phe Ser Ser Cys
  65             70             75             80

```

```

Arg Glu Gly Ser Glu His Tyr Leu Phe Phe Phe Phe Ser Trp Ser
      85             90             95

```

```

Gln Asp Cys Thr Arg Gln Trp Pro Asn Leu Val Glu Phe Ser Leu Pro
  100            105            110

```

```

Ser Phe Ala Asp Asp Ser Ala Leu Cys Gln Val Leu Glu Pro Gln Arg
  115            120            125

```

40

Trp Val Ser Pro Ser Pro Cys Pro Gln Glu Ala His Gly Gln Gly Asn
 130 135 140

Val Val Gly Ile Ser Asn Arg Gly Gln Leu Pro Ser Gly Leu Leu Val
 145 150 155 160

Ala Ala Gly Pro Tyr Gly Ala Leu Met
 165

<210> 57
 <211> 995
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (852)

<400> 57
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 gtgagccaag atcgaccac tgcactccag cctgggtgac agagcgagac tctgtctcaa 180
 aaaaaaaaaa aaaaaagaaa agaaaaaaac ctattgccta cctcccaagg gcaaattgcag 240
 cctggtgttt ggctccaagt ctgottcagc tttggctccc atcactccgc tttccttttg 300
 cctcaactta agatcttgcc acatgtacac ttcccataac attccagctg agaggctttt 360
 gtatacgagg ggtttttttt tgtttgtttt gccwagaatg atcctccctg gtgaatctta 420
 gcttaaatca ccaggcagtt aagcaggctt ttctctatga ttccaacccc actttgtata 480
 tttctgtgat tagtcttgaa catcccatgt tgtactgttt acctctctca ctggacttag 540
 aaattctgaa gaacagaaac aaaaagtttt ctctttctct gtatgttctt tttttgttgt 600
 tattattatt gacttggtat atcttctttc agatgtattt tcttttattc tcaacacaaa 660
 gtaattttta catgatcttt ctgggccaaa attttcttat ctgtaaaatg aagatgttg 720
 actaggattc agggcttctt aactaaagaa ttcaatagat gatgctggga caagtgtata 780
 tctacctgta aaggaatgaa gttggacccc ttctcctac tatacacaaa aattaactca 840
 aaatggatca tngacctaaa cataagagct aaaactataa gactttcaga agaaaacaca 900
 ggagtaagtc ttcattgacct tggattaagg aatggttgct tagatatgac acccaaaaaa 960
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa 995

<210> 58
 <211> 72
 <212> PRT
 <213> Homo sapiens

<400> 58
 Met Leu Tyr Cys Leu Pro Leu Ser Leu Asp Leu Glu Ile Leu Lys Asn
 1 5 10 15

Arg Asn Lys Lys Phe Ser Leu Ser Leu Tyr Val Leu Phe Leu Leu Leu
 20 25 30

Leu Leu Leu Thr Trp Tyr Ile Phe Phe Gln Met Tyr Phe Leu Leu Phe
 35 40 45

Ser Thr Gln Ser Asn Phe Asn Met Ile Phe Leu Gly Gln Asn Phe Leu
 50 55 60

Ile Cys Lys Met Lys Met Leu Asp
 65 70

<210> 59
 <211> 1038

<212> DNA

<213> Homo sapiens

<400> 59

```

gacggcctca ccatgatgaa acgggcagct gctgctgcag tgggaggagg taagttaccc 60
ggatcgcttg tctccaggcc ctcaoctagc ctgggtccccg ggctgctggg agaacgcaga 120
gatgaggcgc tgggctggct ctcaoctcc acttccgaag ctgcccagat agcctgagtg 180
agccacagca tcaaaatact ccagggaata gctcactccc attcctgacc cagcttctct 240
tctagtcctt atgtcgaaata agcataggag gaagatcggt tgaaagarga tttgcagcta 300
aactccacgt ggcttatttc acatttatgc gtggacacac acacacacac acacacacac 360
acacaaattt gagaccaatg aagggtattg acttcctcag catcacacag caagttagag 420
acaaaccagg gccatggctg gtccttctat gacatctttg cttcacctgg ctccacactc 480
caccttttct tcaccagaag accactaagt tgccatctct gtattgctca agctgacagt 540
ctcgggaaac tgtcaaggaa ttctaagcg gggggcgggg ggaagggtcc cttctcctga 600
gcccacctct gcactcagct tctctctccc acagccctgg cagtgggggc tgtgcccgtg 660
gtgctcagtg ccatgggctt cactggggca ggaatcgccg cgtcctccat agcagccaag 720
atgatgtccg cagcagccat tgccaacggg ggtggtgttt ctgctgggag cctggtggct 780
actctgcagt ccgtgggggc agctggactc tccacatcat ccaacatcct cctggcctct 840
gttgggtcag tgtkgggggc gtgctkgggg aattcacctt cttcttctct ccagctgaa 900
ccgaggcta aagaagatga ggcaagagaa aatgtacccc aaggtgaacc tccaaaaccc 960
ccactcaagt cagagaaaca tgaggaataa aggtcacatg cagatgcata aaaaaaaaaa 1020
aaaaaaaaaa aaaaaaaaaa                                     1038

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<210> 60

<211> 105

<212> PRT

<213> Homo sapiens

<220>

<221> UNSURE

<222> (61)

<220>

<221> UNSURE

<222> (65)

<400> 60

```

Met Gly Phe Thr Gly Ala Gly Ile Ala Ala Ser Ser Ile Ala Ala Lys
 1               5               10               15

Met Met Ser Ala Ala Ala Ile Ala Asn Gly Gly Gly Val Ser Ala Gly
 20               25               30

Ser Leu Val Ala Thr Leu Gln Ser Val Gly Ala Ala Gly Leu Ser Thr
 35               40               45

Ser Ser Asn Ile Leu Leu Ala Ser Val Gly Ser Val Xaa Gly Ala Cys
 50               55               60

Xaa Gly Asn Ser Pro Ser Ser Ser Leu Pro Ala Glu Pro Glu Ala Lys
 65               70               75               80

Glu Asp Glu Ala Arg Glu Asn Val Pro Gln Gly Glu Pro Pro Lys Pro
 85               90               95

Pro Leu Lys Ser Glu Lys His Glu Glu
 100               105

```

<210> 61

<211> 1060

<212> DNA

<213> Homo sapiens

<400> 61

```

gaggagacca ggacagctgc tgagacctct aagaagtcca gatactaaga gcaaagatgt 60
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gaggcctgcc cgtgccccctg gaccagaccc tgcccttgaa tgtgaatcca gccctgccct 180
tgagtcccac aggtcttgca ggaagcttga caaatgccct cagcaatggc ctgctgtctg 240
ggggcctggt gggcattctg gaaaaccttc cgctcctgga catcctgaag cctggaggag 300
gtactttctg tggcctcctt gggggactgc ttggaaaagt gacgtcagtg attcctggcc 360
tgaacaacat cattgacata aaggteactg acccccagct gctggaactt ggccttgtgc 420
agagccctga tggccaccgt ctctatgtca ccctccctct cggcataaag ctccaagtga 480
atacgcacct ggtcggtgca agtctgttga ggctggctgt gaagctggac atcactgcag 540
aaatcttagc tgtgagagat aagcaggaga ggatccacct ggtccttggg gactgcaccc 600
attcccctgg aagcctgcaa atttctctgc ttgatggact tggccccctc cccattcaag 660
gtctttctgga cagcctcaca gggatcttga ataaagtcct gcctgagttg gttcagggca 720
acgtgtgccc tctggtcaat gaggttctca gaggcttgga catcaccctg gtgcatgaca 780
ttgttaacat gctgatccac ggactacagt ttgtcatcaa ggtctaagcc ttccaggaag 840
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cttcccagtg ctcacagatg gctggcccat gtgctggaag atgacacagt tgccttctct 960
ccgaggaacc tgccccctct cctttccac caggcgtgtg taacatccca tgtgcctcac 1020
ctaataaaat ggctcttctt ctgcaaaaaa aaaaaaaaaa 1060

```

<210> 62

<211> 256

<212> PRT

<213> Homo sapiens

<400> 62

```

Met Phe Gln Thr Gly Gly Leu Ile Val Phe Tyr Gly Leu Leu Ala Gln
  1             5             10             15

Thr Met Ala Gln Phe Gly Gly Leu Pro Val Pro Leu Asp Gln Thr Leu
      20             25             30

Pro Leu Asn Val Asn Pro Ala Leu Pro Leu Ser Pro Thr Gly Leu Ala
      35             40             45

Gly Ser Leu Thr Asn Ala Leu Ser Asn Gly Leu Leu Ser Gly Gly Leu
      50             55             60

Leu Gly Ile Leu Glu Asn Leu Pro Leu Leu Asp Ile Leu Lys Pro Gly
      65             70             75             80

Gly Gly Thr Ser Gly Gly Leu Leu Gly Gly Leu Leu Gly Lys Val Thr
      85             90             95

Ser Val Ile Pro Gly Leu Asn Asn Ile Ile Asp Ile Lys Val Thr Asp
      100            105            110

Pro Gln Leu Leu Glu Leu Gly Leu Val Gln Ser Pro Asp Gly His Arg
      115            120            125

Leu Tyr Val Thr Ile Pro Leu Gly Ile Lys Leu Gln Val Asn Thr Pro
      130            135            140

Leu Val Gly Ala Ser Leu Leu Arg Leu Ala Val Lys Leu Asp Ile Thr
      145            150            155            160

Ala Glu Ile Leu Ala Val Arg Asp Lys Gln Glu Arg Ile His Leu Val
      165            170            175

```

43

Leu Gly Asp Cys Thr His Ser Pro Gly Ser Leu Gln Ile Ser Leu Leu
 180 185 190

Asp Gly Leu Gly Pro Leu Pro Ile Gln Gly Leu Leu Asp Ser Leu Thr
 195 200 205

Gly Ile Leu Asn Lys Val Leu Pro Glu Leu Val Gln Gly Asn Val Cys
 210 215 220

Pro Leu Val Asn Glu Val Leu Arg Gly Leu Asp Ile Thr Leu Val His
 225 230 235 240

Asp Ile Val Asn Met Leu Ile His Gly Leu Gln Phe Val Ile Lys Val
 245 250 255

<210> 63

<211> 992

<212> DNA

<213> Homo sapiens

<400> 63

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ttctcaacct tgacaccatt gacatttttg actgggtaat tctttgttct gcagagctgt 180
cctttgcact gtaggagatt tactaatatc cctggcctct acccagtagt accactagca 240
cctattcccc acccagcgtg tctccagata ttgtcaaata tcccatcggg tgcaaaatga 300
tccttggtca agatctgttg cccaagatgt tacaggtaac aatgaccaca ttgaaattg 360
ttttcccttt cattttaccc tgtgaaagca tctctcctag agccttgcaa gaggcagggtg 420
acattgtgtc catatttctt cctgtttcag aacttctgtt tcacaacaat ttctctctcg 480
ctacaagtat tctttcactc agcactgggg aagttgggaa cagctggtca ccatcatccc 540
tttaatcaac tcacacctgt ttaaagagtgt tttctgattt gaccttcac ccttagttta 600
ctgggggttaa aaaaagtctc agcaattttc attatttctc gtgggtctca ttatcaaacc 660
tttacttatt tgggcatatt tctctggggt ttcttctagt ttctgcctta caagcaatgc 720
tgttctgtaa atttattgaa aactctggaa catttcacct ttagagatgg aggatggaag 780
gattggtacc agaagagggc taagatacgt tttctgtctt gagctgaaag cacagtctac 840
tctccttcgt tttgtcgatg agaaagtga ggccagaggg gaggtgacat gtttagagtc 900
accagctgg ttagtgacag aaaaagcgtg agagttgtct aggattcctg ccactttcaa 960
taaagacctg acttggaataa aaaaaaaaaa aa 992
```

<210> 64

<211> 82

<212> PRT

<213> Homo sapiens

<400> 64

Met Ile Pro Gly Gln Asp Leu Leu Pro Lys Met Leu Gln Val Thr Met
 1 5 10 15

Thr Thr Phe Glu Ile Val Phe Pro Phe Ile Leu Pro Cys Glu Ser Ile
 20 25 30

Ser Pro Arg Ala Leu Gln Glu Ala Gly Asp Ile Val Ser Ile Phe Leu
 35 40 45

Pro Val Ser Glu Leu Leu Phe His Asn Asn Phe Ser Leu Ala Thr Ser
 50 55 60

Ile Leu Ser Leu Ser Thr Gly Glu Val Gly Asn Ser Trp Ser Pro Ser
 65 70 75 80

Ser Leu

44

<210> 65
 <211> 1095
 <212> DNA
 <213> Homo sapiens

<400> 65
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 gagatttcct gttgaagctc tcaagtgttt ccatctgcag aaaaaaacca gactttctgc 120
 ctgatcatcc cattgtactg caaaaaccag aaaacaacca aagttttaag tagcatttta 180
 agaacagatg aatttaagtt tggacatctg caaatgaggt ggatctagca acaataactg 240
 taatggactg tgacaattca atttattctt aattttgatg gttggctatt tgacttctct 300
 aaaaatgaga aagagctatt ttaaaatata aagaattttc taatcagttt cagctttgca 360
 ggaggtttcc tgcataaatt gggaagtaac actggaaagt aggaatttgg ttagtgaagt 420
 gggaagactg tatatttata atttgcatac tacttgcaat tttttgtttt tcatcacttg 480
 taataatgga atggaaatgt aagctgtaaa gactctcaaa tataaaatat ttgctacagt 540
 gtatatatgg tacataattg cttgttgctt ttaaagttcc ttctgttggt ctgcttccca 600
 ctgatttcat accagctcat gaatggatca ttacagtctc tccagaggct tagaatgatt 660
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 tttcagatat atgattgggtc tctaggtttt tgataataat atggtcttaa attcataatt 780
 actagcagag attgataatt tggaaacaat ggtagtgaat gaaactgaag ttgaaaaacg 840
 gctgctactt atgtcactaa tcagaccata tgaatagcag aagttgagca atttcaaagt 900
 aaaactgata tttttatttc caaaggaatt tagacatttg aaaataattg acatacatta 960
 agttttaatt cgataatttc ttatatatgg atgaacaatt tttgggttta agcttttaatt 1020
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 aaaaaaaaa aaaaa 1095

<210> 66
 <211> 68
 <212> PRT
 <213> Homo sapiens

<400> 66
 Met Val His Asn Cys Leu Leu Leu Lys Phe Leu Leu Leu Phe Cys
 1 5 10 15
 Phe Pro Leu Ile Ser Tyr Gln Leu Met Asn Gly Ser Leu Gln Ser Leu
 20 25 30
 Gln Arg Leu Arg Met Ile Gln Asn Val Gln Cys Ile Val Leu Asn Lys
 35 40 45
 Gln Glu Ala Glu Phe Leu Met Gly Ile Ser Phe Gln Ile Tyr Asp Trp
 50 55 60
 Ser Leu Gly Phe
 65

<210> 67
 <211> 831
 <212> DNA
 <213> Homo sapiens

<400> 67
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 cctgggaaag aggggctgag gcctgaactg ggccaaagga gaggcagct cagttcgcac 180
 acaacagcac ccagccctgt ccccttgctg cctctaccca gccctgggca gttccctcaa 240
 cagagctctg cagccccaag tggcagctgc tggctcaaag ctgggactac atgaaagtct 300
 gaaaagagaa tgagaaggag gtggcgcaag agcctggacg cacgtgtggg aggccgtttt 360
 gtgcagcgct attgtgctcc ccgggcgggc atgkctcgc gctccgtggc tctgttggtg 420

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ccccrcgtgc ggggggtgtgc tkgtggccct gtgggcctgt agggcaaccc atgccaactg 480
cggaaaagta accagcacca tacaccccc ccaacacaaa actggtcatt tttttttttt 540
gttggtcattg ttattaggaa gcaaaaaaat gtacagttac aagaatcatt ttccaaacag 600
agggttaaata tgagctgaaa agtgtaaaaa aggaagagga acatcacttt acaaactcatt 660
aaattaaaca aataaacaaa cagaacccaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a          831

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<210> 68
 <211> 50
 <212> PRT
 <213> Homo sapiens

<220>
 <221> UNSURE
 <222> (29)

<220>
 <221> UNSURE
 <222> (39)

<220>
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<400> 68
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Val Ala Leu Leu Val Pro Xaa Val Arg Gly Cys Ala Xaa Gly Pro Val
 35 40 45

Gly Leu
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<210> 69
 <211> 1893
 <212> DNA
 <213> Homo sapiens

<400> 69
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<210> 70

<211> 309

<212> PRT

<213> Homo sapiens

<400> 70

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Met Ser Phe Leu Ile Asp Ser Ser Ile Met Ile Thr Ser Gln Ile Leu
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```

```

Phe Phe Gly Phe Gly Trp Leu Phe Phe Met Arg Gln Leu Phe Lys Asp
      20                      25                      30

```

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Tyr Glu Ile Arg Gln Tyr Val Val Gln Val Ile Phe Ser Val Thr Phe
  35                      40                      45

```

```

Ala Phe Ser Cys Thr Met Phe Glu Leu Ile Ile Phe Glu Ile Leu Gly
  50                      55                      60

```

```

Val Leu Asn Ser Ser Ser Arg Tyr Phe His Trp Lys Met Asn Leu Cys
  65                      70                      75                      80

```

```

Val Ile Leu Leu Ile Leu Val Phe Met Val Pro Phe Tyr Ile Gly Tyr
      85                      90                      95

```

```

Phe Ile Val Ser Asn Ile Arg Leu Leu His Lys Gln Arg Leu Leu Phe
  100                      105                      110

```

```

Ser Cys Leu Leu Trp Leu Thr Phe Met Tyr Phe Phe Trp Lys Leu Gly
  115                      120                      125

```

```

Asp Pro Phe Pro Ile Leu Ser Pro Lys His Gly Ile Leu Ser Ile Glu
  130                      135                      140

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```

Gln Leu Ile Ser Arg Val Gly Val Ile Gly Val Thr Leu Met Ala Leu
  145                      150                      155                      160

```

```

Leu Ser Gly Phe Gly Ala Val Asn Cys Pro Tyr Thr Tyr Met Ser Tyr
  165                      170                      175

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```

Phe Leu Arg Asn Val Thr Asp Thr Asp Ile Leu Ala Leu Glu Arg Arg
  180                      185                      190

```

```

Leu Leu Gln Thr Met Asp Met Ile Ile Ser Lys Lys Lys Arg Met Ala
  195                      200                      205

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47

Met Ala Arg Arg Thr Met Phe Gln Lys Gly Glu Val His Asn Lys Pro
 210 215 220

Ser Gly Phe Trp Gly Met Ile Lys Ser Val Thr Thr Ser Ala Ser Gly
 225 230 235 240

Ser Glu Asn Leu Thr Leu Ile Gln Gln Glu Val Asp Ala Leu Glu Glu
 245 250 255

Leu Ser Arg Gln Leu Phe Leu Glu Thr Ala Asp Leu Tyr Ala Thr Lys
 260 265 270

Glu Arg Ile Glu Tyr Ser Lys Thr Phe Lys Gly Lys Tyr Leu Ile Ser
 275 280 285

Trp Leu Leu Phe Leu Tyr Leu Leu Cys Leu Glu Asn Phe His Glu Tyr
 290 295 300

His Gln Tyr Cys Ile
 305

<210> 71
 <211> 1424
 <212> DNA
 <213> Homo sapiens

<400> 71
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<210> 72
 <211> 70
 <212> PRT
 <213> Homo sapiens

<400> 72
 Met Thr Ser Glu His Ala Thr Leu Arg Ser Leu Ser Ala Leu Pro Thr
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48.

Phe Pro Asn Pro Ala Val Ser Thr Pro Gly Leu Trp Arg Leu Tyr Arg
 20 25 30

Tyr Glu Met Gln Arg Ala Cys Gly Leu Gly Val Ser Val Val Trp Gly
 35 40 45

Cys Gly Gly Ser Pro Val Trp His Gly Cys Glu Gly Ala Val Glu Asp
 50 55 60

Arg Leu Ser Val Leu Pro
 65 70

<210> 73
 <211> 1726
 <212> DNA
 <213> Homo sapiens

<400> 73
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<210> 74
 <211> 133
 <212> PRT
 <213> Homo sapiens

<400> 74
 Met Val Ser Ser Trp Pro Ala Arg Lys Ala Ser Leu Leu Cys Val Cys
 1 5 10 15

Ala Val Leu Val Leu Pro Trp Arg Thr Leu Gly Ser Pro Val Ile Leu
 20 25 30

49.

Ala Arg Arg Pro Gly Ala Trp Val Pro Ser Trp Lys Gly Thr Ser Tyr
 35 40 45

Thr Pro Gln Pro His Phe Pro Thr Asn Phe Tyr Met Pro Trp Glu Asn
 50 55 60

Leu Leu His Val Gly Cys Pro Leu Pro Leu Phe Gln Gln Cys Pro Val
 65 70 75 80

Leu Leu Ile Asn Leu Arg Pro Ala Pro His Thr Leu Pro Cys Ala Ser
 85 90 95

Ala Ser Arg Tyr Ser Arg Gln Pro Asn Val Val Glu Ala Arg Trp Ile
 100 105 110

Pro Gly Ser Ser Trp Pro Met Asp Val Ser His His Ser Ile Leu Glu
 115 120 125

Thr Glu Lys Arg Ser
 130

<210> 75
 <211> 927
 <212> DNA
 <213> Homo sapiens

<400> 75
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<210> 76
 <211> 142
 <212> PRT
 <213> Homo sapiens

<400> 76
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Pro Arg Ser Gln Pro Ile Asn Leu Asn His Tyr Ala Thr Lys Lys Ser
 20 25 30

Val Ala Glu Ser Met Leu Asp Val Ala Leu Phe Met Ser Asn Ala Met
 35 40 45

Arg Leu Lys Ala Val Leu Glu Gln Gly Pro Ser Ser His Tyr Tyr Thr
 50 55 60

50.

Thr Leu Val Thr Leu Ile Ser Leu Ser Leu Leu Leu Gln Val Val Ile
65 70 75 80

Gly Val Leu Leu Val Val Ile Ala Arg Leu Asn Leu Asn Glu Val Glu
85 90 95

Lys Gln Trp Arg Leu Asn Gln Leu Asn Asn Ala Ala Thr Ile Leu Val
100 105 110

Phe Phe Thr Val Val Ile Asn Val Phe Ile Thr Ala Phe Gly Ala His
115 120 125

Lys Thr Gly Phe Leu Ala Ala Arg Ala Ser Arg Asn Pro Leu
130 135 140

<210> 77

<211> 1660

<212> DNA

<213> Homo sapiens

<400> 77

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<210> 78

<211> 447

<212> PRT

<213> Homo sapiens

<400> 78

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51,

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 20 25 30
 Gln Ser Gly Thr Pro Gly Met Ala Ser Leu Ser Leu Glu Thr Met Arg
 35 40 45
 Gln Leu Gly Ser Leu Gln Arg Leu Asn Thr Leu Ser Gln Tyr Ser Arg
 50 55 60
 Tyr Gly Phe Gly Lys Ser Phe Asn Ser Leu Trp Met His Gly Leu Leu
 65 70 75 80
 Pro Pro His Ser Ser Leu Pro Trp Met Arg Pro Arg Glu His Glu Thr
 85 90 95
 Gln Gln Tyr Glu Tyr Ser Leu Pro Val His Pro Pro Pro Leu Pro Ser
 100 105 110
 Gln Pro Ser Leu Lys Pro Gln Gln Pro Gly Leu Lys Pro Phe Leu Gln
 115 120 125
 Ser Ala Ala Ala Thr Thr Asn Gln Ala Thr Ala Leu Lys Glu Ala Leu
 130 135 140
 Gln Pro Pro Ile His Leu Gly His Leu Pro Leu Gln Glu Gly Glu Leu
 145 150 155 160
 Pro Leu Val Gln Gln Gln Val Ala Pro Ser Asp Lys Pro Pro Lys Pro
 165 170 175
 Glu Leu Pro Gly Val Asp Phe Ala Asp Pro Gln Gly Pro Ser Leu Pro
 180 185 190
 Gly Met Asp Phe Pro Asp Pro Gln Gly Pro Ser Leu Pro Gly Leu Asp
 195 200 205
 Phe Ala Asp Pro Gln Gly Ser Thr Ile Phe Gln Ile Ala Arg Leu Ile
 210 215 220
 Ser His Gly Pro Met Pro Gln Asn Lys Gln Ser Pro Leu Tyr Pro Gly
 225 230 235 240
 Met Leu Tyr Val Pro Phe Gly Ala Asn Gln Leu Asn Ala Pro Ala Arg
 245 250 255
 Leu Gly Ile Met Ser Ser Glu Glu Val Ala Gly Gly Arg Glu Asp Pro
 260 265 270
 Met Ala Tyr Gly Ala Met Phe Pro Gly Phe Gly Gly Met Arg Pro Gly
 275 280 285
 Phe Glu Gly Met Pro His Asn Pro Ala Met Gly Gly Asp Phe Thr Leu
 290 295 300
 Glu Phe Asp Ser Pro Val Ala Ala Thr Lys Gly Pro Glu Asn Glu Glu
 305 310 315 320
 Gly Gly Ala Gln Gly Ser Pro Met Pro Glu Ala Asn Pro Asp Asn Leu
 325 330 335
 Glu Asn Pro Ala Phe Leu Thr Glu Leu Glu Pro Ala Pro His Ala Gly
 340 345 350

Leu Leu Ala Leu Pro Lys Asp Asp Ile Pro Gly Leu Pro Arg Ser Pro
 355 360 365

Ser Gly Lys Met Lys Gly Leu Pro Ser Val Thr Pro Ala Ala Ala Asp
 370 375 380

Pro Leu Met Thr Pro Glu Leu Ala Asp Val Tyr Arg Thr Tyr Asp Ala
 385 390 395 400

Asp Met Thr Thr Ser Val Asp Phe Gln Glu Glu Ala Thr Met Asp Thr
 405 410 415

Thr Met Ala Pro Asn Ser Leu Gln Thr Ser Met Pro Gly Asn Lys Ala
 420 425 430

Gln Glu Pro Glu Met Met His Asp Ala Trp His Phe Gln Glu Pro
 435 440 445

<210> 79

<211> 2036

<212> DNA

<213> Homo sapiens

<400> 79

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<210> 80

53.

<211> 81
 <212> PRT
 <213> Homo sapiens

<400> 80
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 1 5 10 15
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 20 25 30
 Leu Leu His Pro Thr Val Ala Ser Val Val Trp Thr Trp Trp Leu Leu
 35 40 45
 His Pro Thr Gln Gly Asn Ser Val Leu Leu His Pro Thr Asp Cys Trp
 50 55 60
 Glu Arg Ala Ser Gly Thr Phe Leu Trp Gly Ile Ile Leu Phe Cys Leu
 65 70 75 80
 Leu

<210> 81
 <211> 3465
 <212> DNA
 <213> Homo sapiens

<400> 81
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 aaaatatgag gagaagacct ttcagacata tgaccttcat caaatgggtcc cagtggaga 240
 agagtaataa atgaaattaa tcaagaccaa gaaactagga gggcagcggg aggtaggga 300
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<210> 82

<211> 51

<212> PRT

<213> Homo sapiens

<400> 82

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Met Met Ile Arg Ala Ala His Leu His Gly Leu Val Ser Leu Leu Leu
  1             5             10             15

```

```

Met Trp Ile Tyr Ala Thr Asp Leu His Phe Gly His His Lys Lys Tyr
      20             25             30

```

```

Cys Cys Ala Ser Pro Thr Pro Thr Pro Thr Pro Leu Val Tyr Ser Leu
      35             40             45

```

```

Lys Trp Tyr
      50

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<210> 83

<211> 808

<212> DNA

<213> Homo sapiens

<400> 83

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attggaggaa ctggaagctg ctgcattggg ggtaaccata gcaacaataa acctcaaacc 180
tagcccaact ctttttttta ttactttttt agagacaagg tcttgctctg ttgccaggc 240
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ctcctgcttc agcctttgta ggagattggt cagggtgggt ggagaaatta taggaaagac 360
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aggcagccaa attcttatct gaagcctgag agcaaagggc agataacagg ggagttgtat 480
aggaacttac ctagataaat ttgtttattc ctgtgtccag aaaccaacct ttgatcattc 540
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55

tgctccaagc ctttgtcatt aaatttgtgc taaataaatg tgagggccac cagcttaagg 660
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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 780
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 808

<210> 84
 <211> 45
 <212> PRT
 <213> Homo sapiens

<400> 84
 Met Leu Thr Met Phe Ile Ala His Lys Leu Cys Leu Leu Gln Ala Phe
 1 5 10 15
 Val Ile Lys Phe Val Leu Asn Lys Cys Glu Gly His Gln Leu Lys Gly
 20 25 30
 Thr Ala Asn Ser Leu Arg Pro Leu Val Leu Ala Val Pro
 35 40 45

<210> 85
 <211> 1024
 <212> DNA
 <213> Homo sapiens

<400> 85
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 catgccataa acatccttga acccatgcag gaaagcccat cccatattct gaaaaaatgc 180
 caaattaggt ttttctttct ttttggaat cagtcattac agtaaccgaa accattgggt 240
 tcagcgaaaa tggaaagatt tagctgaatg tagtcagtcc aattaagttg gatgcaactg 300
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 cagcgatggt ttctaaacat cgtccagtgt tgactggctt ccttactttg cacagtgaac 540
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 aaaa 1024

<210> 86
 <211> 64
 <212> PRT
 <213> Homo sapiens

<400> 86
 Met Ser Gln Gln Gln His Trp Pro Asn Leu Arg Pro Ser Leu Leu Ala
 1 5 10 15
 His His Met Cys Thr Val Leu Phe Ala Val Val Leu Ile Ile His Pro
 20 25 30
 Ser Leu Cys His Pro Gln Ala Ser Leu Gly Val Lys Arg Lys Leu Ser
 35 40 45

56

Thr Asp Thr Ala Met Arg Ser His Val Leu Met Pro Ser Gly Ala Gln
 50 55 60

<210> 87
 <211> 867
 <212> DNA
 <213> Homo sapiens

<400> 87
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 aaagcatagt tgaggcatat tttttcataa ttatatactt atctgtttat tgcccatgga 180
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<210> 88
 <211> 51
 <212> PRT
 <213> Homo sapiens

<400> 88
 Met Glu Asn Ile Cys Val Glu Val Phe Leu Leu Leu Phe Val Thr Ile
 1 5 10 15

Phe Leu Ile Cys Ser Lys Glu Asn Ala Ala Ile Leu His Ser Leu Trp
 20 25 30

Lys Glu Thr Lys Gln Asn Lys Thr His Ser Lys Pro Ala Val Leu Leu
 35 40 45

Ser Asp Lys
 50

<210> 89
 <211> 1797
 <212> DNA
 <213> Homo sapiens

<400> 89
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 caggagatta tagaagccat gcagtagaca agatccaaaa tacgttgcat tgttggtgtg 480
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 gttgttttat aaaggatgat accattatag agtcagaaat gggagtcgtt gcaggaattt 660

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<210> 90

<211> 245

<212> PRT

<213> Homo sapiens

<400> 90

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Met Ala Ser Pro Ser Arg Arg Leu Gln Thr Lys Pro Val Ile Thr Cys
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```

```

Phe Lys Ser Val Leu Leu Ile Tyr Thr Phe Ile Phe Trp Ile Thr Gly
  20             25             30

```

```

Val Ile Leu Leu Ala Val Gly Ile Trp Gly Lys Val Ser Leu Glu Asn
  35             40             45

```

```

Tyr Phe Ser Leu Leu Asn Glu Lys Ala Thr Asn Val Pro Phe Val Leu
  50             55             60

```

```

Ile Ala Thr Gly Thr Val Ile Ile Leu Leu Gly Thr Phe Gly Cys Phe
  65             70             75             80

```

```

Ala Thr Cys Arg Ala Ser Ala Trp Met Leu Lys Leu Tyr Ala Met Phe
  85             90             95

```

```

Leu Thr Leu Val Phe Leu Val Glu Leu Val Ala Ala Ile Val Gly Phe
  100            105            110

```

```

Val Phe Arg His Glu Ile Lys Asn Ser Phe Lys Asn Asn Tyr Glu Lys
  115            120            125

```

```

Ala Leu Lys Gln Tyr Asn Ser Thr Gly Asp Tyr Arg Ser His Ala Val
  130            135            140

```

```

Asp Lys Ile Gln Asn Thr Leu His Cys Cys Gly Val Thr Asp Tyr Arg
  145            150            155            160

```

```

Asp Trp Thr Asp Thr Asn Tyr Tyr Ser Glu Lys Gly Phe Pro Lys Ser
  165            170            175

```

```

Cys Cys Lys Leu Glu Asp Cys Thr Pro Gln Arg Asp Ala Asp Lys Val
  180            185            190

```

58

Asn Asn Glu Gly Cys Phe Ile Lys Val Met Thr Ile Ile Glu Ser Glu
 195 200 205

Met Gly Val Val Ala Gly Ile Ser Phe Gly Val Ala Cys Phe Gln Leu
 210 215 220

Ile Gly Ile Phe Leu Ala Tyr Cys Leu Ser Arg Ala Ile Thr Asn Asn
 225 230 235 240

Gln Tyr Glu Ile Val
 245

<210> 91
 <211> 1992
 <212> DNA
 <213> Homo sapiens

<400> 91
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 accagagaat atttttaaat tcacgtttta ttgcatctac aaaattaaaa gttttgcaga 1860
 acacatgcta catttcaaca aagatcattt cctccttaat ttaactacaa atgttaatta 1920
 cacttatctt taaataaaat gagtttttcc tttaaaaaaa aaaaaaaaaa aaaaaaaaaa 1980
 aaaaaaaaaa aa 1992

<210> 92
 <211> 556
 <212> PRT
 <213> Homo sapiens

<400> 92
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	20						25					30			
Ile	Leu	Met	Lys	Lys	Met	Gly	Ile	Lys	Ser	Gly	Phe	Thr	Phe	Trp	Asn
	35					40					45				
Leu	Val	Phe	Leu	Leu	Thr	Val	Ser	Cys	Val	Lys	Gly	Phe	Ile	Tyr	Thr
	50				55					60					
Cys	Gly	Gly	Thr	Leu	Lys	Gly	Leu	Asn	Gly	Thr	Ile	Glu	Ser	Pro	Gly
	65				70					75					80
Phe	Pro	Tyr	Gly	Tyr	Pro	Asn	Gly	Ala	Asn	Cys	Thr	Trp	Val	Ile	Ile
			85					90					95		
Ala	Glu	Glu	Arg	Asn	Arg	Ile	Gln	Ile	Val	Phe	Gln	Ser	Phe	Ala	Leu
		100					105					110			
Glu	Glu	Glu	Tyr	Asp	Tyr	Leu	Ser	Leu	Tyr	Asp	Gly	His	Pro	His	Pro
	115					120					125				
Thr	Asn	Phe	Arg	Thr	Arg	Leu	Thr	Gly	Phe	His	Leu	Pro	Pro	Pro	Val
	130				135					140					
Thr	Ser	Thr	Lys	Ser	Val	Phe	Ser	Leu	Arg	Leu	Thr	Ser	Asp	Phe	Ala
	145				150					155					160
Val	Ser	Ala	His	Gly	Phe	Lys	Val	Tyr	Tyr	Glu	Glu	Leu	Gln	Ser	Ser
			165					170					175		
Ser	Cys	Gly	Asn	Pro	Gly	Val	Pro	Pro	Lys	Gly	Val	Leu	Tyr	Gly	Thr
		180					185					190			
Arg	Phe	Asp	Val	Gly	Asp	Lys	Ile	Arg	Tyr	Ser	Cys	Val	Thr	Gly	Tyr
	195					200					205				
Ile	Leu	Asp	Gly	His	Pro	Gln	Leu	Thr	Cys	Ile	Ala	Asn	Ser	Val	Asn
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Thr	Ala	Ser	Trp	Asp	Phe	Pro	Val	Pro	Ile	Cys	Arg	Ala	Glu	Asp	Ala
	225				230					235					240
Cys	Gly	Gly	Thr	Met	Arg	Gly	Ser	Ser	Gly	Ile	Ile	Ser	Ser	Pro	Ser
			245				250					255			
Phe	Pro	Asn	Glu	Tyr	His	Asn	Asn	Ala	Asp	Cys	Thr	Trp	Thr	Ile	Val
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Ala	Glu	Pro	Gly	Asp	Thr	Ile	Ser	Leu	Ile	Phe	Thr	Asp	Phe	Gln	Met
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Glu	Glu	Lys	Tyr	Asp	Tyr	Leu	Glu	Ile	Glu	Gly	Ser	Glu	Pro	Pro	Thr
	290				295					300					
Ile	Trp	Leu	Ser	Gly	Met	Asn	Ile	Pro	Pro	Pro	Ile	Ile	Ser	Asn	Lys
	305				310					315					320
Asn	Trp	Leu	Arg	Leu	His	Phe	Val	Thr	Asp	Ser	Asn	His	Arg	Tyr	Arg
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 Arg Gly Phe Lys Leu Phe Pro Gly Lys Asp Asn Ser Asn Lys Phe Ser
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 405 410 415
 Ala Lys Ser Ile Thr Cys Gln Arg Ile Ala Glu Val Phe Ala Ala Trp
 420 425 430
 Ser Asp His Arg Pro Val Cys Lys Val Lys Thr Cys Gly Ser Asn Leu
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 450 455 460
 Asp Ser Asn Ala Gln Cys Val Trp Val Ile Thr Ala Val Asn Thr Asn
 465 470 475 480
 Lys Val Ile Gln Ile Asn Phe Glu Glu Phe Asp Leu Glu Ile Gly Tyr
 485 490 495
 Asp Thr Leu Thr Ile Gly Asp Gly Gly Glu Val Gly Asp Pro Arg Thr
 500 505 510
 Val Leu Gln Val Leu Thr Gly Ser Phe Val Pro Asp Leu Ile Val Ser
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 <212> DNA
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<210> 94

<211> 399

<212> PRT

<213> Homo sapiens

<400> 94

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      20              25              30

Val Arg Pro Ser Pro Ala Lys Arg Arg Leu Ser Thr Leu Ile Leu His
      35              40              45

Gly Gly Gly Thr Val Cys Arg Val Gln Glu Pro Gly Ala Val Leu Leu
      50              55              60

Ala Gln Pro Gly Glu Ala Leu Ala Glu Ala Ser Gly Asp Phe Ile Ser
      65              70              75              80

Thr Gln Tyr Ile Leu Asp Cys Val Glu Arg Asn Glu Arg Leu Glu Leu
      85              90              95

Glu Ala Tyr Arg Leu Gly Pro Ala Ser Ala Ala Asp Thr Gly Ser Glu
      100              105              110

Ala Lys Pro Gly Ala Leu Ala Glu Gly Ala Ala Glu Pro Glu Pro Gln
      115              120              125

Arg His Ala Gly Arg Ile Ala Phe Thr Asp Ala Asp Asp Val Ala Ile
      130              135              140

Leu Thr Tyr Val Lys Glu Asn Ala Arg Ser Pro Ser Ser Val Thr Gly
      145              150              155              160

Asn Ala Leu Trp Lys Ala Met Glu Lys Ser Ser Leu Thr Gln His Ser
      165              170              175

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 His Lys Tyr Leu Leu Gly Asp Ala Pro Val Ser Pro Ser Ser Gln Lys
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 Pro Gln Asn Lys Arg Thr Pro Asp Leu Pro Glu Glu Glu Tyr Val Lys
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 245 250 255
 Ala Thr Arg Glu Phe Glu Glu Val Val Val Asp Glu Ser Pro Pro Asp
 260 265 270
 Phe Glu Ile His Ile Thr Met Cys Asp Asp Asp Pro Pro Thr Pro Glu
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 Lys Val Ser Gln Pro Glu Val Gly Ala Ala Ile Lys Ile Ile Arg Gln
 305 310 315 320
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 325 330 335
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 340 345 350
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 355 360 365
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 385 390 395

<210> 95

<211> 1427

<212> DNA

<213> Homo sapiens

<400> 95

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 <213> Homo sapiens

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 Ser Leu Leu Glu Trp Ile Asp Asp Leu Leu Trp Gln Ser Thr Leu Gln
 35 40 45
 Phe Phe His Pro Asp Glu Val Leu Phe Phe Tyr Thr Tyr Ser Leu Ser
 50 55 60
 Tyr Ser Arg Ser Pro Ala Thr Leu Tyr Pro Ser Leu Ile Ile Ser Arg
 65 70 75 80
 Ile Pro Ser Thr Ser Pro Thr Pro Ser Ser Pro Ser Pro Ile Leu Pro
 85 90 95
 Met His Phe Pro Leu Phe Leu Xaa Leu Tyr Arg Cys Pro Cys Pro Ala
 100 105 110
 Ser Pro Xaa Gly Asn Phe Pro His Leu Pro Ile Pro Pro Asn Leu Phe
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Gln

<210> 97
 <211> 2482
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure

<222> (1663)

<400> 97

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<210> 98

<211> 413

<212> PRT

<213> Homo sapiens

<400> 98

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      20                      25                      30

Lys Val Pro Arg Ile Val Ser Glu Arg Thr Phe His Leu Thr Ser Pro
      35                      40                      45

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65

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 Val Tyr Ser Gly His Gln Trp Val Asp Val His Gly Val Gln Lys Asp
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<210> 99

<211> 2054

<212> DNA

<213> Homo sapiens

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<221> unsure

<222> (650)

<400> 99

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<212> PRT

<213> Homo sapiens

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 20             25             30

Thr Met Leu Asn Gly Leu Leu Ile Lys Asp Ser Ser Pro Pro Met Leu
 35             40             45

Leu Xaa Gln Val Xaa Lys Thr Ala Xaa Xaa Asp Xaa Phe Xaa Tyr Gln
 50             55             60

Xaa Cys Phe Met Xaa Ser Val Phe Asp His Phe Pro Glu Ile Leu Phe
 65             70             75             80

Ile His Xaa Thr Tyr Asn Pro Arg Gly Lys Val Leu Tyr Xaa Phe Leu
 85             90             95

Val Asp Gly Pro Xaa Val Gln Leu Glu Gly Xaa Leu Ala Arg Ala Val
100             105             110

Tyr Phe Ala Ile Pro Ala Lys Glu Asp Thr Glu Gly Leu Ala Gln Met
115             120             125

Phe Gln Val Phe Lys Lys Phe Asn Pro Ala Trp Glu Arg Val Cys Thr
130             135             140

Ile Leu Val Asp Pro His Phe Leu Pro Leu Pro Ile Leu Ala Met Glu
145             150             155             160

Phe Pro Thr Ala Glu Val Leu Leu Ser Ala Phe His Ile Cys Lys Phe
165             170             175

Leu Gln Ala Lys Phe Tyr Gln Leu Ser Leu Glu Arg Pro Val Glu Arg
180             185             190

Xaa Leu Leu Thr Ser Leu Gln Ser Thr Met Cys Ser Ala Thr Ala Gly
195             200             205

Asn Leu Arg Lys Leu Tyr Thr Leu Leu Ser Asn Cys Ile Pro Pro Ala
210             215             220

Lys Leu Pro Glu Leu His Ser His Trp Leu Leu Asn Asp Arg Ile Trp
225             230             235             240

Leu Ala His Arg Trp Arg Ser Arg Ala Glu Ser Ser His Tyr Phe Gln
245             250             255

Ser Leu Glu Val Thr Thr His Ile Leu Ser Gln Phe Phe Gly Thr Thr
260             265             270

Pro Ser Glu Lys Gln Gly Met Ala Ser Leu Phe Arg Tyr Met Gln Gln
275             280             285

Asn Ser Ala Asp Lys Ala Asn Phe Asn Gln Gly Leu Cys Ala Gln Asn
290             295             300

Asn His Ala Pro Pro Asp Ile Ile Pro Glu Ser Pro Lys Leu Glu Gln
305             310             315             320

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69,

Leu Val Glu Ser His Ile Gln His Ser Leu Asn Ala Ile Cys Thr Gly
 325 330 335
 Pro Ala Ala Gln Leu Cys Leu Gly Glu Leu Ala Val Val Gln Lys Ser
 340 345 350
 Thr His Leu Ile Gly Ser Gly Ser Glu Lys Met Asn Ile Gln Ile Leu
 355 360 365
 Glu Asp Thr His Lys Val Gln Pro Xaa Pro Pro Ala Ser Cys Xaa Cys
 370 375 380
 Tyr Phe Asn Gln Ala Phe His Leu Pro Cys Arg His Ile Leu Ala Met
 385 390 395 400
 Leu Ser Ala Arg Arg Gln Val Leu Gln Pro Asp Met Leu Pro Ala Gln
 405 410 415
 Trp Thr Ala Gly Cys Ala Thr Ser Leu Asp Ser Ile Leu Gly Ser Lys
 420 425 430
 Trp Ser Glu Thr Leu Asp Lys His Leu Ala Val Thr His Leu Thr Glu
 435 440 445
 Glu Val Gly Gln Leu Leu Gln His Cys Thr Lys Glu Glu Phe Glu Arg
 450 455 460
 Arg Tyr Ser Thr Leu Arg Glu Leu Ala Asp Ser Trp Ile Gly Pro Tyr
 465 470 475 480
 Glu Gln Val Gln Leu
 485

<210> 101
 <211> 700
 <212> DNA
 <213> Homo sapiens

<400> 101
 ggggggtttga aaggagctgc tcttgctggc tccggtgcag gggatgaatg ccagtgaatg 60
 ccagtgttca gcagggtcc tgccaggcgg cactccaggg tccggcccaa ggtgactgtc 120
 ctgaactatg cctccccgat aaccgcagtc agccggccac tgaatgagat ggtccttgacc 180
 ccactgacag agcaggaggg ggaagcctac ctggagaagt gtggcagcgt gcggcggcac 240
 acggtggcca atgcccactc ggacatccag ctgctggcca tggccaccat gatgcactcs 300
 ggcctggggg aggaggccar cagtgagaac aagtkcctgc tctgcccacc carcttcccc 360
 ccgccccacc sgcagtgtc cagtkagccc aacatcaccg acaaccctga cggactggag 420
 gagggggcca ggggcagcca ggagggtcg gagctgaact gtgcttccct cagctgagtc 480
 gccaccctg ggcctttcca tctcctgtt tgcaaccagg atgrggaccc ctccatctcc 540
 gtggattact gaggggggct cttgctttat gcgatgctgc cttatttcc ttaggggtact 600
 gtccctggtca aaatgacct aggggaaacc gttgtgttaa acctttttat tttggaaaaa 660
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 700

<210> 102
 <211> 139
 <212> PRT
 <213> Homo sapiens

<220>
 <221> UNSURE
 <222> (88)

<220>
 <221> UNSURE
 <222> (93)

<220>
 <221> UNSURE
 <222> (99)

<220>
 <221> UNSURE
 <222> (105)

<220>
 <221> UNSURE
 <222> (110)

<400> 102

Met Pro Val Phe Ser Arg Ala Pro Ala Arg Arg His Ser Arg Val Arg
 1 5 10 15

Pro Lys Val Thr Val Leu Asn Tyr Ala Ser Pro Ile Thr Ala Val Ser
 20 25 30

Arg Pro Leu Asn Glu Met Val Leu Thr Pro Leu Thr Glu Gln Glu Gly
 35 40 45

Glu Ala Tyr Leu Glu Lys Cys Gly Ser Val Arg Arg His Thr Val Ala
 50 55 60

Asn Ala His Ser Asp Ile Gln Leu Leu Ala Met Ala Thr Met Met His
 65 70 75 80

Ser Gly Leu Gly Glu Glu Ala Xaa Ser Glu Asn Lys Xaa Leu Leu Leu
 85 90 95

Pro Pro Xaa Phe Pro Pro Pro His Xaa Gln Cys Ser Ser Xaa Pro Asn
 100 105 110

Ile Thr Asp Asn Pro Asp Gly Leu Glu Glu Gly Ala Arg Gly Ser Gln
 115 120 125

Glu Gly Ser Glu Leu Asn Cys Ala Ser Leu Ser
 130 135

<210> 103
 <211> 658
 <212> DNA
 <213> Homo sapiens

<400> 103

cccgtcagtt ctgctcacgt gaggtgcttc atgaaccctc tctctgctca ctacctgtaa 60
 cagtgggtgca aatgaatggt tataccattc ttcgaggatc ccatcaggga caagtgcagg 120
 gcagtggccc atcagggtgg tgtctacaag ggaactttgg tccatctctc ttcagtgact 180
 ggaggagccc ctggccagca tccttccaca castgctgct tgcaggcaca ggactggccc 240
 ccaccttccc ggcctccagc gtggtggcaa gcctgcctga acctgggagt tcctcagggc 300
 ccacttccaa atgccactga gccacagcag ggaacaagaa tcaaagagca cccacccgc 360
 caccatgcc tatggccccc tccaagggtg tcagtggggt tcagtgggcc ctacaggccc 420
 tcctcgaatc cagccccatc tgcaagtccc aaagaaactt ttctaaagtt tctggaatgc 480
 ggggtgcaacc ctactggtt tttgccccat ttttatgttc cattcatttc actgggattc 540
 tgagaggggg aagataaact tgggttcaag ctaccctagc tgaccagga gttccatgga 600
 aacagaattc tgaaaaaaaa aaaaaataaa taaataaata attaaaaaaaa aaaaaaaa 658

71,

<210> 104
 <211> 155
 <212> PRT
 <213> Homo sapiens

<220>
 <221> UNSURE
 <222> (46)

<400> 104

Met Phe Ile Pro Ile Phe Glu Asp Pro Ile Arg Asp Lys Cys Arg Ala
 1 5 10 15

Val Ala His Gln Gly Gly Val Tyr Lys Gly Thr Leu Val His Leu Ser
 20 25 30

Ser Val Thr Gly Gly Ala Pro Gly Gln His Pro Ser Thr Xaa Cys Cys
 35 40 45

Leu Gln Ala Gln Asp Trp Pro Pro Pro Ser Arg Pro Pro Ala Trp Trp
 50 55 60

Gln Ala Cys Leu Asn Leu Gly Val Pro Gln Gly Pro Leu Pro Asn Ala
 65 70 75 80

Thr Glu Pro Gln Gln Gly Thr Arg Ile Lys Glu His Pro Thr Arg His
 85 90 95

Pro Cys Leu Trp Pro Pro Pro Arg Val Ser Val Gly Phe Ser Gly Pro
 100 105 110

Tyr Arg Pro Ser Ser Asn Pro Ala Pro Ser Ala Ser Pro Lys Glu Thr
 115 120 125

Phe Leu Lys Phe Leu Glu Cys Gly Cys Asn Pro His Trp Phe Leu Pro
 130 135 140

His Phe Tyr Val Pro Phe Ile Ser Leu Gly Phe
 145 150 155

<210> 105
 <211> 836
 <212> DNA
 <213> Homo sapiens

<400> 105

atatctttat gattttctcc ttttctagtt tgggattgac ttaagcaaata tagatttttaa 60
 ggaccaagca actaacagaa aatacatcat ggctgtacat ttggagggga aaaaaatagt 120
 gtatcataga ataattcatc tctgtcata tactttctcc cagttttgac ccagcaaaac 180
 aaagagaagc ctcactagac aaaatgcacc ttattcttac aagggtggaa acaatacatt 240
 gaaatagcca ggtacttgaa atgggagaag gataatgaac agcgaggaca agacagttgg 300
 ccatttttcc gcgtctattg ctctctttct tattttctgca cctttattgc ttctaattggg 360
 ttcaactatg tgtgtttata tttttaggaa tggaggaaat accttaggaa gcagatgaat 420
 tattgatcat atacagaaat gatagagaca gtaggaaata tgtttgatgg aagccctgtg 480
 tatatatattt tggggggagg ggcttgaagt cacttggtac acagggtttt gggtaaggat 540
 tggagaaaat gggaataaat ttttctagaa gcagaactat gttctgaatt ggcatctttg 600
 aaagggggaa taaaccctta agtgggtggg actgtaactt tgtttgggga gacaaagagg 660
 agactctctt gagaccttta ttatcaggat gaggtttaaa gtcagatccc aaggaaaaaa 720
 cagccctagt gaaacttcca agctctttga gagttgactt tttgggtttg atagaaaatg 780
 gaagtaagga taatagattt gactgtgtgc catggttagtg gaaaaaaaaa aaaaaa 836

72,

<210> 106
 <211> 47
 <212> PRT
 <213> Homo sapiens

<400> 106
 Met Asn Ser Glu Asp Lys Thr Val Gly His Phe Ser Ala Ser Ile Ala
 1 5 10 15
 Leu Phe Leu Ile Ser Ala Pro Leu Leu Leu Leu Met Gly Ser Thr Met
 20 25 30
 Cys Val Tyr Ile Phe Arg Asn Gly Gly Asn Thr Leu Gly Ser Arg
 35 40 45

<210> 107
 <211> 1581
 <212> DNA
 <213> Homo sapiens

<400> 107
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 tagcccagca cagagccacc ggaacatcaa gatcctagag gacgaacccc acagtaagga 180
 tgagacccca ctgtgtaccc ttctggactg gcaggattct cttgccaaagc gctgcgtctg 240
 tgtgtccaat accattcgaa gcctgtcatt tgtgccaggc aatgactttg agatgtccaa 300
 acaccaggg ctgctgctca tcctgggcaa gctgatcctg ctgcaccaca agcaccagga 360
 acggaagcag gcaccactaa cttatgaaaa ggaggaggaa caggaccaag ggtgagctgc 420
 aacaaaatgg agtgggtggg ggactgcttg gagatgctcc gggaaaacac cttggttaca 480
 ctcgccaaca tctcggggca gttggaccta tctccatacc ccgagagcat ttgcctgcct 540
 gtccctggacg gactcctaca ctgggcagtt tgcccttcag ctgaagccca ggaccctttt 600
 tccaccctgg gccccaatgc cgtcctttcc ccgagagac tggctcttga aaccctcagc 660
 aaactcagca tccaggacaa caatgtggac ctgattcttg ccacaccccc cttcagccgc 720
 ctggagaagt tgtatagcac tatggtgcgc ttctcagtg accgaaagaa cccggtgtgc 780
 cgggagatgg ctgtggtact gctggccaac ctggctcagg gggacagcct ggcagctcgt 840
 gccattgcag tgcagaaggg cagtatcggc aacctcctgg gcttcctaga ggacagcctt 900
 gccgccacac agttccagca gagccaggcc agcctcctcc acatgcagaa cccacccttt 960
 gagccaacta gtgtggacat gatgcggcgg gctgcccgcg cgctgcttgc cttggccaag 1020
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 ttagaaactg actgttgccc tttatttatg caaaaccacc tcagaatcca gtttaccctg 1260
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 taaccaaaagt tactgttggt tacagtgagt ttggggaaaa aaaataaaat aaaaatggct 1500
 ttcccagtc ttgcatcaac gggatgccac atttcataac tgtttttaat ggtaaaaaaa 1560
 aaaaaaaaaa aaaaaaaaaa a 1581

<210> 108
 <211> 240
 <212> PRT
 <213> Homo sapiens

<400> 108
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 Val Thr Leu Ala Asn Ile Ser Gly Gln Leu Asp Leu Ser Pro Tyr Pro
 20 25 30

Glu Ser Ile Cys Leu Pro Val Leu Asp Gly Leu Leu His Trp Ala Val
 35 40 45
 Cys Pro Ser Ala Glu Ala Gln Asp Pro Phe Ser Thr Leu Gly Pro Asn
 50 55 60
 Ala Val Leu Ser Pro Gln Arg Leu Val Leu Glu Thr Leu Ser Lys Leu
 65 70 75 80
 Ser Ile Gln Asp Asn Asn Val Asp Leu Ile Leu Ala Thr Pro Pro Phe
 85 90 95
 Ser Arg Leu Glu Lys Leu Tyr Ser Thr Met Val Arg Phe Leu Ser Asp
 100 105 110
 Arg Lys Asn Pro Val Cys Arg Glu Met Ala Val Val Leu Leu Ala Asn
 115 120 125
 Leu Ala Gln Gly Asp Ser Leu Ala Ala Arg Ala Ile Ala Val Gln Lys
 130 135 140
 Gly Ser Ile Gly Asn Leu Leu Gly Phe Leu Glu Asp Ser Leu Ala Ala
 145 150 155 160
 Thr Gln Phe Gln Gln Ser Gln Ala Ser Leu Leu His Met Gln Asn Pro
 165 170 175
 Pro Phe Glu Pro Thr Ser Val Asp Met Met Arg Arg Ala Ala Arg Ala
 180 185 190
 Leu Leu Ala Leu Ala Lys Val Asp Glu Asn His Ser Glu Phe Thr Leu
 195 200 205
 Tyr Glu Ser Arg Leu Leu Asp Ile Ser Val Ser Pro Leu Met Asn Ser
 210 215 220
 Leu Val Ser Gln Val Ile Cys Asp Val Leu Phe Leu Ile Gly Gln Ser
 225 230 235 240

<210> 109

<211> 1684

<212> DNA

<213> Homo sapiens

<400> 109

ctgcctgatt tgggaagcgc tgcaaggaca accggctggg gtccttgccg gccgcggctc 60
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 tgtttcgctg gtcctgttga tgcctggccc ctgtgatggg ctgtttcact ccctatacag 180
 aagtgtttcc atgccaccta agggagactc aggacagcca ttattttotca ccccttacat 240
 tgaagctggg aagatccaaa aaggaagaga attgagtttg gtcgggtcctt tcccaggact 300
 gaacatgaag agttatgccg gcttcctcac cgtgaataag acttacaaca gcaacctctt 360
 cttctgggtc ttcccagctc agatacagcc agaagatgcc ccagtagtto tctgggtaca 420
 ggggtgggccc ggaggttcat ccatgttttg actctttgtg gaacatgggc cttatgttgt 480
 cacaagtaac atgaccttgc gtgacagaga cttccccctgg accacaacgc tctccatgct 540
 ttacattgac aatccagtgg gcacaggctt cagttttact gatgataccc acggatatgc 600
 agtcaatgag gacgatgtag cacgggattt atacagtga ctaattcagt tttccagat 660
 atttcctgaa tataaaaata atgactttta tgtcactggg gagtcttatg cagggaaata 720
 tgtgccagcc attgcacacc tcatccattc cctcaaccct gtgagagagg tgaagatcaa 780
 cctgaacgga attgctattg gagatggata ttctgatccc gaatcaatta tagggggcta 840
 tgcagaattc ctgtacctaa ttggcttgtt ggatgagaag caaaaaaagt acttcagaa 900

74,

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gcagtgccat gaatgcatag aacacatcag gaagcagaac tggtttgagg cctttgaaat 960
actggataaa ctactagatg gcgacttaac aagtgaccc tcttacttcc agaatgttac 1020
aggatgtagt aattactata actttttgcg gtgcacggaa cctgaggatc agctttacta 1080
tgtgaaattt ttgtcactcc cagaggtgag acaagccatc cacgtgggga atcagacttt 1140
taatgatgga actatagttg aaaagtactt gcgagaagat acagtacagt cagttaagcc 1200
atggttaact gaaatcatga ataattataa ggttctgac tacaatggcc aactggacat 1260
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tggttacatc cggcaagcgg gtgacttcca tcaggtaatt attcgagggtg gaggacatat 1440
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aggatgggat ccttatgttg gataaactac cttcccaaaa gagaacatca gaggttttca 1560
ttgctgaaaa gaaaatcgta aaaacagaaa atgtcatagg aataaaaaaa ttatcttttc 1620
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aaaa
1684

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<210> 110

<211> 476

<212> PRT

<213> Homo sapiens

<400> 110

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Met Val Gly Ala Met Trp Lys Val Ile Val Ser Leu Val Leu Leu Met
  1             5             10             15

Pro Gly Pro Cys Asp Gly Leu Phe His Ser Leu Tyr Arg Ser Val Ser
  20             25             30

Met Pro Pro Lys Gly Asp Ser Gly Gln Pro Leu Phe Leu Thr Pro Tyr
  35             40             45

Ile Glu Ala Gly Lys Ile Gln Lys Gly Arg Glu Leu Ser Leu Val Gly
  50             55             60

Pro Phe Pro Gly Leu Asn Met Lys Ser Tyr Ala Gly Phe Leu Thr Val
  65             70             75             80

Asn Lys Thr Tyr Asn Ser Asn Leu Phe Phe Trp Phe Phe Pro Ala Gln
  85             90             95

Ile Gln Pro Glu Asp Ala Pro Val Val Leu Trp Leu Gln Gly Gly Pro
 100             105             110

Gly Gly Ser Ser Met Phe Gly Leu Phe Val Glu His Gly Pro Tyr Val
 115             120             125

Val Thr Ser Asn Met Thr Leu Arg Asp Arg Asp Phe Pro Trp Thr Thr
 130             135             140

Thr Leu Ser Met Leu Tyr Ile Asp Asn Pro Val Gly Thr Gly Phe Ser
 145             150             155             160

Phe Thr Asp Asp Thr His Gly Tyr Ala Val Asn Glu Asp Asp Val Ala
 165             170             175

Arg Asp Leu Tyr Ser Ala Leu Ile Gln Phe Phe Gln Ile Phe Pro Glu
 180             185             190

Tyr Lys Asn Asn Asp Phe Tyr Val Thr Gly Glu Ser Tyr Ala Gly Lys
 195             200             205

Tyr Val Pro Ala Ile Ala His Leu Ile His Ser Leu Asn Pro Val Arg
 210             215             220

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75.

Glu Val Lys Ile Asn Leu Asn Gly Ile Ala Ile Gly Asp Gly Tyr Ser
 225 230 235 240
 Asp Pro Glu Ser Ile Ile Gly Gly Tyr Ala Glu Phe Leu Tyr Leu Ile
 245 250 255
 Gly Leu Leu Asp Glu Lys Gln Lys Lys Tyr Phe Gln Lys Gln Cys His
 260 265 270
 Glu Cys Ile Glu His Ile Arg Lys Gln Asn Trp Phe Glu Ala Phe Glu
 275 280 285
 Ile Leu Asp Lys Leu Leu Asp Gly Asp Leu Thr Ser Asp Pro Ser Tyr
 290 295 300
 Phe Gln Asn Val Thr Gly Cys Ser Asn Tyr Tyr Asn Phe Leu Arg Cys
 305 310 315 320
 Thr Glu Pro Glu Asp Gln Leu Tyr Tyr Val Lys Phe Leu Ser Leu Pro
 325 330 335
 Glu Val Arg Gln Ala Ile His Val Gly Asn Gln Thr Phe Asn Asp Gly
 340 345 350
 Thr Ile Val Glu Lys Tyr Leu Arg Glu Asp Thr Val Gln Ser Val Lys
 355 360 365
 Pro Trp Leu Thr Glu Ile Met Asn Asn Tyr Lys Val Leu Ile Tyr Asn
 370 375 380
 Gly Gln Leu Asp Ile Ile Val Ala Ala Ala Leu Thr Glu Arg Ser Leu
 385 390 395 400
 Met Gly Met Asp Trp Lys Gly Ser Gln Glu Tyr Lys Lys Ala Glu Lys
 405 410 415
 Lys Val Trp Lys Ile Phe Lys Ser Asp Ser Glu Val Ala Gly Tyr Ile
 420 425 430
 Arg Gln Ala Gly Asp Phe His Gln Val Ile Ile Arg Gly Gly Gly His
 435 440 445
 Ile Leu Pro Tyr Asp Gln Pro Leu Arg Ala Phe Asp Met Ile Asn Arg
 450 455 460
 Phe Ile Tyr Gly Lys Gly Trp Asp Pro Tyr Val Gly
 465 470 475

<210> 111

<211> 750

<212> DNA

<213> Homo sapiens

<400> 111

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 cctggcgctg tgctagcttt ctttacagc tgtttacaga caaggcaggc ctgaggcaga 180
 tggccactgc tcttgtgatg tttgctcaga ggaatatgaa cattttatatt ttgaaaaggg 240
 atgatgtggt ttttgccagg tgtttataat taatccttta atattatggg tattaacctc 300
 ttaaacaatga atgaattctt gattgtttta acacagtacc taagactaat gctttctgtg 360

76.

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gacaccactg agctctgect caactccacc ctctgcgacc ggaggactat gcccctagta 420
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tctgagacag gatcgttgtc cctacaggag gaacagtggc cttgcttctt agacgggtctt 540
cactgtgtgt tttaaaacaa caacaacaac aacaacaaca taaaactctt ttgacctgta 600
acttaaagat cataaacttc aggcaataat attttctgtg taagctttta aaattatttt 660
tggggatcat agcttgtttt attttgtgct ataaaattaa cagtattaaa tgacttatat 720
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<210> 112

<211> 89

<212> PRT

<213> Homo sapiens

<400> 112

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Met Val Ile Asn Leu Leu Asn Met Asn Glu Phe Leu Ile Val Leu Thr
  1             5             10             15

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Gln Tyr Leu Arg Leu Met Leu Ser Val Asp Thr Thr Glu Leu Cys Leu
      20             25             30

```

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Asn Ser Thr Leu Cys Asp Arg Arg Thr Met Pro Leu Val Thr Ala Val
    35             40             45

```

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Gly Val Asp Ala Val Leu Val Leu Phe Ser Lys Gly Ala Glu Gly Gln
    50             55             60

```

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Val Ser Glu Thr Gly Ser Leu Ser Leu Gln Glu Glu Gln Trp Pro Cys
    65             70             75             80

```

```

Phe Leu Asp Gly Leu His Cys Val Phe
      85

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<210> 113

<211> 2156

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (1353)

<400> 113

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gtgggttttg tttgcatgtc cctgataaat aatgatgttg accatctact catgtgcttg 180
ttggctatth gcatggcgtg tttggagaaa cgtctgttca agggcctttgc cttttttttt 240
tgagacagar tcttactccg ttgccccarg ctggagtkcg gtggtgaggg gtgcaactgca 300
acatccgcct tccagggtca agcgattctt gtgcctcagc ctcccaaaga gctgggatta 360
caaaagtgca gtttgcccat ttttaatcga ttttgttctt gagttggagt tttttgtata 420
ttcaggctgt taacccttta tgagatagat ggtttgcaca tagtctcttc cattctatag 480
gatatcattt ctgttaatag attcctttgc tgtgcagaaa ctttttagtt tgaggtcatt 540
ccatttgtct atttttactt tcgttgccct tgctgttggt gtcattgttca agaaatcatt 600
gccaaagacca atgtcgtgaa gtctttccct ttgttttctt ctaagggttt tacagtttca 660
agtctgtggt tgggtcttgc atcgggtttg agttagtttt tgtgtatgat gtaaggtaag 720
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cttgacagtg gtaatttatt tgcttctttt tcttattagt ccttttgcc actttaaata 1020
attaattttg ttaattttta gttttctgtt atttttagttc attaatttca ttgcttctt 1080
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77

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gtggcacgat ctcagctcac tgcaacctcc acctcccagg ttcaagtgat tctcctgtct 1200
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tgagagaagca tgatgactcc atgggggtaca gaatttagaa catccttgtc agattgagtc 1680
tatggtgatg tgtcttaagt cgtcccttag tctttttttt cctaatacgt ctgtcaaatt 1740
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<210> 114

<211> 94

<212> PRT

<213> Homo sapiens

<400> 114

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      20              25              30
Leu Lys Val Val Ser Ser Val Phe Pro Ser Phe Asn Ser Ser Ser Val
      35              40              45
Ala Val Arg Leu Gln Ile Pro Gly Cys Leu Thr Trp Val Pro Phe His
      50              55              60
Met Gly Val Ser Gln Gln Thr Ala Leu Gln Ile Val His Thr Phe Ser
      65              70              75              80
Lys Thr Asn Asn Gly Thr Gly Gly Lys Pro Met Pro Ile Tyr
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<210> 115

<211> 3941

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (2895)

<400> 115

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<210> 116

<211> 70

<212> PRT

<213> Homo sapiens

<400> 116

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Val His Cys Gly Met Cys Asn Leu Arg Tyr Phe Glu Phe Ser Thr Phe
 20 25 30

Leu Leu Ser Leu Ser Leu Ile Thr Tyr Cys Phe Trp Asp Pro Pro His
 35 40 45

Arg Gly Ser His Ser Leu Ser Leu Glu His Thr Pro Leu Asp Phe Leu
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Glu Trp Gly Leu Leu Arg
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<210> 117

<211> 1779

<212> DNA

<213> Homo sapiens

<400> 117

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<210> 118

<211> 109

<212> PRT

<213> Homo sapiens

<400> 118

80

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 Gly Val Gln Lys Asp Gln Cys Lys Ser Lys Thr Ser Cys Ala Cys Pro
 35 40 45
 Arg Gly Pro Gln Arg Gln Asp Ala Pro Thr Gln Lys Glu Thr Pro Lys
 50 55 60
 Leu Ala Trp Pro Lys Gly Gly Arg Thr Gln Gly Gly Cys Arg Asn Ser
 65 70 75 80
 Ser Lys Asn Asn Asp Val Ile Arg Gln Met Cys His Cys Ala Gly Ala
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 Gly Trp Val Trp Gln Ala His Leu Gly Tyr Ala Lys Leu
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<210> 119
 <211> 1170
 <212> DNA
 <213> Homo sapiens

<400> 119
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<210> 120
 <211> 183
 <212> PRT
 <213> Homo sapiens

<400> 120
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 Phe Gln His Arg Glu Arg Val Ala Met His Tyr Gln Met Ser Val Thr
 20 25 30

81.

Leu Lys Tyr Glu Ile Lys Lys Leu Ile Tyr Val His Leu Val Ile Trp
 35 40 45

Leu Leu Leu Val Ala Lys Met Ser Val Gly His Leu Arg Leu Leu Ser
 50 55 60

His Asp Gln Val Ala Met Pro Tyr Gln Trp Glu Tyr Pro Tyr Leu Leu
 65 70 75 80

Ser Ile Leu Pro Ser Leu Leu Gly Leu Leu Ser Phe Pro Arg Asn Asn
 85 90 95

Ile Ser Tyr Leu Val Leu Ser Met Ile Ser Met Gly Leu Phe Ser Ile
 100 105 110

Ala Pro Leu Ile Tyr Gly Ser Met Glu Met Phe Pro Ala Ala Gln Gln
 115 120 125

Leu Tyr Arg His Gly Lys Ala Tyr Arg Phe Leu Phe Gly Phe Ser Ala
 130 135 140

Val Ser Ile Met Tyr Leu Val Leu Val Leu Ala Val Gln Val His Ala
 145 150 155 160

Trp Gln Leu Tyr Tyr Ser Lys Lys Leu Leu Asp Ser Trp Phe Thr Ser
 165 170 175

Thr Gln Glu Lys Lys His Lys
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<210> 121

<211> 1127

<212> DNA

<213> Homo sapiens

<400> 121

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<210> 122

<211> 140

<212> PRT

<213> Homo sapiens

82

<400> 122

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Gln Ile Leu Tyr Asn Ile Lys Gln Glu Tyr Lys Arg Met Gln Lys Arg
 20 25 30

Arg His Leu Glu Thr Ser Phe Gln Gln Thr Asp Pro Cys Cys Thr Ser
 35 40 45

Asp Ala Gln Pro His Ala Phe Leu Leu Ser Gly Pro Ala Ser Pro Gly
 50 55 60

Thr Ser Ser Ala Ala Ser Ser Pro Leu Lys Lys Glu Gln Pro Leu Phe
 65 70 75 80

Thr Leu Arg Gln Val Gly Met Ile Cys Glu Arg Leu Leu Lys Glu Arg
 85 90 95

Glu Glu Lys Val Arg Glu Glu Tyr Glu Glu Ile Leu Asn Thr Lys Leu
 100 105 110

Ala Glu Gln Tyr Asp Ala Phe Val Lys Phe Thr His Asp Gln Ile Met
 115 120 125

Arg Arg Tyr Gly Glu Gln Pro Ala Ser Tyr Val Ser
 130 135 140

<210> 123

<211> 806

<212> DNA

<213> Homo sapiens

<400> 123

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<210> 124

<211> 55

<212> PRT

<213> Homo sapiens

<220>

<221> UNSURE

<222> (46)

<400> 124

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83.

Leu Ala Ser Arg Arg Phe Gln Ala Trp Gly Ser Thr Lys Val Val Arg
 20 25 30

Thr Phe Gln Asp Ile Pro Gln Asn Tyr Val Tyr Val Gln Xaa Ala Leu
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Trp Phe Ala Ile Glu Gly Val
 50 55

<210> 125

<211> 1783

<212> DNA

<213> Homo sapiens

<400> 125

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<210> 126

<211> 136

<212> PRT

<213> Homo sapiens

<220>

<221> UNSURE

<222> (108)

<400> 126

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Gln Leu Cys Ser Leu Cys Leu Gln Phe Lys Gly Ala Pro Trp Lys Lys
 35 40 45

Cys Asn Asn Ser Leu Thr Cys Asp Trp Tyr Leu Thr Ala Thr Thr Pro
 50 55 60

Gly Gln Gln Trp Leu Thr Val Asp Lys Asp Asn Phe Phe Leu Ser Pro
 65 70 75 80

Lys Pro Asn Ser Leu His Gln Leu Pro Ser Gln Asp Ser Leu Ser Gly
 85 90 95

Pro Tyr Arg Cys Arg Ser Gly Trp Gln Leu Pro Xaa Leu Gly Lys Arg
 100 105 110

Lys Tyr Pro Ile Met Ala Thr Tyr Leu His Leu Gln Leu Leu Pro Val
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His Pro Gln Ser Leu Leu Phe Val
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<210> 127

<211> 3149

<212> DNA

<213> Homo sapiens

<400> 127

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<210> 128

<211> 380

<212> PRT

<213> Homo sapiens

<400> 128

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  1             5             10             15

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Leu Asp Thr Leu Ser Leu Gly Ile His Leu Glu Lys Lys Asn Asp Asp
      20             25             30

```

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His Ser Ser Trp Arg Lys Val Leu Glu Lys Cys Gln Gly Val Val Asp
      35             40             45

```

```

Ile Pro Phe Arg Ser Lys Gly Met Ser Arg Leu Gly Glu Glu Val Asn
      50             55             60

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Gly Glu Ala Thr Glu Ser Gln Gln Lys Pro Arg Asn Lys Lys Ser Lys
      65             70             75             80

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Met Asp Gly Met Val Pro Gly Asn His Gln Gly Arg Asp Pro Arg Lys
      85             90             95

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```

His Lys Arg Lys Pro Leu Gly Val Gly Tyr Ser Ala Arg Lys Ser Pro
      100            105            110

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Leu Tyr Asp Asn Cys Phe Leu His Ala Pro Asp Gly Gln Pro Leu Cys
      115            120            125

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Thr Cys Asp Arg Arg Lys Ala Gln Trp Tyr Leu Asp Lys Gly Ile Gly
      130            135            140

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Glu Leu Val Ser Glu Glu Pro Phe Val Val Lys Leu Arg Phe Glu Pro
      145            150            155            160

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Ala Gly Arg Pro Glu Ser Pro Gly Asp Tyr Tyr Leu Met Val Lys Glu
      165            170            175

```

Asn Leu Cys Val Val Cys Gly Lys Arg Asp Ser Tyr Ile Arg Lys Asn
 180 185 190
 Val Ile Pro His Glu Tyr Arg Lys His Phe Pro Ile Glu Met Lys Asp
 195 200 205
 His Asn Ser His Asp Val Leu Leu Leu Cys Thr Ser Cys His Ala Ile
 210 215 220
 Ser Asn Tyr Tyr Asp Asn His Leu Lys Gln Gln Leu Ala Lys Glu Phe
 225 230 235 240
 Gln Ala Pro Ile Gly Ser Glu Glu Gly Leu Arg Leu Leu Glu Asp Pro
 245 250 255
 Glu Arg Arg Gln Val Arg Ser Gly Ala Arg Ala Leu Leu Asn Ala Glu
 260 265 270
 Ser Leu Pro Thr His Arg Lys Glu Glu Leu Leu Gln Ala Leu Arg Glu
 275 280 285
 Phe Tyr Asn Thr Asp Val Val Thr Glu Glu Met Leu Gln Glu Ala Ala
 290 295 300
 Ser Leu Glu Thr Arg Ile Ser Asn Glu Asn Tyr Val Pro His Gly Leu
 305 310 315 320
 Lys Val Val Gln Cys His Ser Gln Gly Gly Leu Arg Ser Leu Met Gln
 325 330 335
 Leu Glu Ser Arg Trp Arg Gln His Phe Leu Asp Ser Met Gln Pro Lys
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 His Leu Pro Gln Gln Trp Ser Val Asp His Asn His Gln Lys Leu Leu
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 Arg Lys Phe Gly Glu Asp Leu Pro Ile Gln Leu Ser
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<210> 129
 <211> 1861
 <212> DNA
 <213> Homo sapiens

<400> 129
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<210> 130
 <211> 571
 <212> PRT
 <213> Homo sapiens

<220>
 <221> UNSURE
 <222> (202)

<220>
 <221> UNSURE
 <222> (504)

<400> 130
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 35 40 45
 Phe Leu Val Glu Leu Tyr Gly Asn Ser Leu Leu Leu Thr Ala Val Tyr
 50 55 60
 Gly Leu Val Val Ala Gly Ser Val Leu Val Leu Gly Ala Ile Ile Gly
 65 70 75 80
 Asp Trp Val Asp Lys Asn Ala Arg Leu Lys Val Ala Gln Thr Ser Leu
 85 90 95
 Val Val Gln Asn Val Ser Val Ile Leu Cys Gly Ile Ile Leu Met Met
 100 105 110
 Val Phe Leu His Lys His Glu Leu Leu Thr Met Tyr His Gly Trp Val
 115 120 125
 Leu Thr Ser Cys Tyr Ile Leu Ile Ile Thr Ile Ala Asn Ile Ala Asn
 130 135 140
 Leu Ala Ser Thr Ala Thr Ala Ile Thr Ile Gln Arg Asp Trp Ile Val
 145 150 155 160

Val Val Ala Gly Glu Asp Arg Ser Lys Leu Ala Asn Met Asn Ala Thr
 165 170 175
 Ile Arg Arg Ile Asp Gln Leu Thr Asn Ile Leu Ala Pro Met Ala Val
 180 185 190
 Gly Gln Ile Met Thr Phe Gly Ser Pro Xaa Ile Gly Cys Gly Phe Ile
 195 200 205
 Ser Gly Trp Asn Leu Val Ser Met Cys Val Glu Tyr Val Leu Leu Trp
 210 215 220
 Lys Val Tyr Gln Lys Thr Pro Ala Leu Ala Val Lys Ala Gly Leu Lys
 225 230 235 240
 Glu Glu Glu Thr Glu Leu Lys Gln Leu Asn Leu His Lys Asp Thr Glu
 245 250 255
 Pro Lys Pro Leu Glu Gly Thr His Leu Met Gly Val Lys Asp Ser Asn
 260 265 270
 Ile His Glu Leu Glu His Glu Gln Glu Pro Thr Cys Ala Ser Gln Met
 275 280 285
 Ala Glu Pro Phe Arg Thr Phe Arg Asp Gly Trp Val Ser Tyr Tyr Asn
 290 295 300
 Gln Pro Val Phe Leu Ala Gly Met Gly Leu Ala Phe Leu Tyr Met Thr
 305 310 315 320
 Val Leu Gly Phe Asp Cys Ile Thr Thr Gly Tyr Ala Tyr Thr Gln Gly
 325 330 335
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 340 345 350
 Gly Ile Met Gly Thr Val Ala Phe Thr Trp Leu Arg Arg Lys Cys Gly
 355 360 365
 Leu Val Arg Thr Gly Leu Ile Ser Gly Leu Ala Gln Leu Ser Cys Leu
 370 375 380
 Ile Leu Cys Val Ile Ser Val Phe Met Pro Gly Ser Pro Leu Asp Leu
 385 390 395 400
 Ser Val Ser Pro Phe Glu Asp Ile Arg Ser Arg Phe Ile Gln Gly Glu
 405 410 415
 Ser Ile Thr Pro Thr Lys Ile Pro Glu Ile Thr Thr Glu Ile Tyr Met
 420 425 430
 Ser Asn Gly Ser Asn Ser Ala Asn Ile Val Pro Glu Thr Ser Pro Glu
 435 440 445
 Ser Val Pro Ile Ile Ser Val Ser Leu Leu Phe Ala Gly Val Ile Ala
 450 455 460
 Ala Arg Ile Gly Leu Trp Ser Phe Asp Leu Thr Val Thr Gln Leu Leu
 465 470 475 480
 Gln Glu Asn Val Ile Glu Ser Glu Arg Gly Ile Ile Asn Gly Val Gln
 485 490 495

Asn Ser Met Asn Tyr Leu Leu Xaa Leu Leu His Phe Ile Met Val Ile
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Leu Ala Pro Asn Pro Glu Ala Phe Gly Leu Leu Val Leu Ile Ser Val
515 520 525

Ser Phe Val Ala Met Gly His Ile Met Tyr Phe Arg Phe Ala Gln Asn
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Thr Leu Gly Asn Lys Leu Phe Ala Cys Gly Pro Asp Ala Lys Glu Val
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Arg Lys Glu Asn Gln Ala Asn Thr Ser Val Val
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<210> 131

<211> 2157

<212> DNA

<213> Homo sapiens

<400> 131

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<210> 132

<211> 270

<212> PRT

<213> Homo sapiens

<400> 132

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Met Asp Pro Gln Gly Gln Thr Leu Leu Leu Phe Leu Phe Val Asp Phe
 35           40           45

His Ser Ala Phe Pro Val Gln Gln Met Glu Ile Trp Gly Val Tyr Thr
 50           55           60

Leu Leu Thr Thr His Leu Asn Ala Ile Leu Val Glu Ser His Ser Val
 65           70           75           80

Val Gln Gly Ser Ile Gln Phe Thr Val Asp Lys Val Leu Glu Gln His
      85           90           95

His Gln Ala Ala Lys Ala Gln Gln Lys Leu Gln Ala Ser Leu Ser Val
    100           105           110

Ala Val Asn Ser Ile Met Ser Ile Leu Thr Gly Ser Thr Arg Ser Ser
    115           120           125

Phe Arg Lys Met Cys Leu Gln Thr Leu Gln Ala Ala Asp Thr Gln Glu
    130           135           140

Phe Arg Thr Lys Leu His Lys Val Phe Arg Glu Ile Thr Gln His Gln
    145           150           155           160

Phe Leu His His Cys Ser Cys Glu Val Lys Gln Leu Thr Leu Glu Lys
    165           170           175

Lys Asp Ser Ala Gln Gly Thr Glu Asp Ala Pro Asp Asn Ser Ser Leu
    180           185           190

Glu Leu Leu Ala Val Leu Lys Gln Pro Ser Gln Pro Thr Ala Ala Gly
    195           200           205

Val Gln Gln Leu Ser His Ser Val Thr Ser Arg Asp Ala Arg Tyr Gln
    210           215           220

Arg Ala Ser Arg Lys Gln Glu Ala Gln Glu Gly Gln Pro Pro His Arg
    225           230           235           240

Gly Asp Ala Ser Ser Ala Leu Cys Gln Gly Pro Glu Pro Val Arg Gly
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    260           265           270

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<210> 133

<211> 1607

<212> DNA

<213> Homo sapiens

<400> 133

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<210> 134

<211> 217

<212> PRT

<213> Homo sapiens

<400> 134

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Met Val Leu Val Asn Thr Ile Tyr Phe Lys Gly Gln Trp Gln Asn Lys
  1             5             10            15

```

```

Phe Gln Val Arg Glu Thr Val Lys Ser Pro Phe Gln Leu Ser Glu Gly
      20             25            30

```

```

Lys Asn Val Thr Val Glu Met Met Tyr Gln Ile Gly Thr Phe Lys Leu
  35             40            45

```

```

Ala Phe Val Lys Glu Pro Gln Met Gln Val Leu Glu Leu Pro Tyr Val
  50             55            60

```

```

Asn Asn Lys Leu Ser Met Ile Ile Leu Leu Pro Val Gly Ile Ala Asn
  65             70            75            80

```

```

Leu Lys Gln Ile Glu Lys Gln Leu Asn Ser Gly Thr Phe His Glu Trp
      85             90            95

```

```

Thr Ser Ser Ser Asn Met Met Glu Arg Glu Val Glu Val His Leu Pro
  100            105            110

```

```

Arg Phe Lys Leu Glu Ile Lys Tyr Glu Leu Asn Ser Leu Leu Lys Pro
  115            120            125

```

```

Leu Gly Val Thr Asp Leu Phe Asn Gln Val Lys Ala Asp Leu Ser Gly
  130            135            140

```


92

Met Ser Pro Thr Lys Gly Leu Tyr Leu Ser Lys Ala Ile His Lys Ser
 145 150 155 160

Tyr Leu Asp Val Ser Glu Glu Gly Thr Glu Ala Ala Ala Ala Thr Gly
 165 170 175

Asp Ser Ile Ala Val Lys Ser Leu Pro Met Arg Ala Gln Phe Lys Ala
 180 185 190

Asn His Pro Phe Leu Phe Phe Ile Arg His Thr His Thr Asn Thr Ile
 195 200 205

Leu Phe Cys Gly Lys Leu Ala Ser Pro
 210 215

<210> 135
 <211> 1537
 <212> DNA
 <213> Homo sapiens

<400> 135
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 graaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa 1537

<210> 136
 <211> 86
 <212> PRT
 <213> Homo sapiens

<400> 136
 Met His Ala Cys Ala Gly Leu Gly Trp Ala Ala Gly Gly Arg Gly Ala
 1 5 10 15

Gly Leu Gly Val Cys Ala Gln Leu Ile Thr Ala Met His Cys Thr Ala
 20 25 30

93

His Val Pro Arg Ala Tyr Arg Asp Pro Thr Leu Phe Arg Ala Phe Leu
 35 40 45

Pro Pro Ala Arg Ala Gln Leu Pro Pro Ala Trp Ala Asn Leu Leu Gln
 50 55 60

Gly Ser Pro Arg Arg Met Gly Thr Arg Lys Ala Val Asp Pro His Leu
 65 70 75 80

Gln Gly Ala Phe Pro Ala
 85

<210> 137
 <211> 1302
 <212> DNA
 <213> Homo sapiens

<400> 137
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<210> 138
 <211> 339
 <212> PRT
 <213> Homo sapiens

<400> 138
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Met Glu Leu Ser Lys Ala Phe Ser Gly Gln Arg Thr Leu Leu Ser Ala
 20 25 30

Ile Leu Ser Met Leu Ser Leu Ser Phe Ser Thr Thr Ser Leu Leu Ser
 35 40 45

Asn Tyr Trp Phe Val Gly Thr Gln Lys Val Pro Lys Pro Leu Cys Glu
 50 55 60

Lys Gly Leu Ala Ala Lys Cys Phe Asp Met Pro Val Ser Leu Asp Gly
 65 70 75 80

Asp Thr Asn Thr Ser Thr Gln Glu Val Val Gln Tyr Asn Trp Glu Thr
 85 90 95
 Gly Asp Asp Arg Phe Ser Phe Arg Ser Phe Arg Ser Gly Met Trp Leu
 100 105 110
 Ser Cys Glu Glu Thr Val Glu Glu Pro Gly Glu Arg Cys Arg Ser Phe
 115 120 125
 Ile Glu Leu Thr Pro Pro Ala Lys Arg Glu Ile Leu Trp Leu Ser Leu
 130 135 140
 Gly Thr Gln Ile Thr Tyr Ile Gly Leu Gln Phe Ile Ser Phe Leu Leu
 145 150 155 160
 Leu Leu Thr Asp Leu Leu Leu Thr Gly Asn Pro Ala Cys Gly Leu Lys
 165 170 175
 Leu Ser Ala Phe Ala Ala Val Ser Ser Val Leu Ser Gly Leu Leu Gly
 180 185 190
 Met Val Ala His Met Met Tyr Ser Gln Val Phe Gln Ala Thr Val Asn
 195 200 205
 Leu Gly Pro Glu Asp Trp Arg Pro His Val Trp Asn Tyr Gly Trp Ala
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 Phe Tyr Met Ala Trp Leu Ser Phe Thr Cys Cys Met Ala Ser Ala Val
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 Thr Thr Phe Asn Thr Tyr Thr Arg Met Val Leu Glu Phe Lys Cys Lys
 245 250 255
 His Ser Lys Ser Phe Lys Glu Asn Pro Asn Cys Leu Pro His His His
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 Gln Cys Phe Pro Arg Arg Leu Ser Ser Ala Ala Pro Thr Val Gly Pro
 275 280 285
 Leu Thr Ser Tyr His Gln Tyr His Asn Gln Pro Ile His Ser Val Ser
 290 295 300
 Glu Gly Val Asp Phe Tyr Ser Glu Leu Arg Asn Lys Gly Phe Gln Arg
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<210> 139

<211> 3184

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (1644)

<400> 139

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<210> 140

<211> 454

<212> PRT

<213> Homo sapiens

<220>

<221> UNSURE

<222> (442)

<400> 140

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Pro Leu Ile Gly Ala Leu Ser Asp Val Trp Gly Arg Lys Pro Phe Leu
 35 40 45

Leu Gly Thr Val Phe Phe Thr Cys Phe Pro Ile Pro Leu Met Arg Ile
 50 55 60

Ser Pro Trp Trp Tyr Phe Ala Met Ile Ser Val Ser Gly Val Phe Ser
 65 70 75 80

Val Thr Phe Ser Val Ile Phe Ala Tyr Val Ala Asp Val Thr Gln Glu
 85 90 95

His Glu Arg Ser Thr Ala Tyr Gly Trp Val Ser Ala Thr Phe Ala Ala
 100 105 110

Ser Leu Val Ser Ser Pro Ala Ile Gly Ala Tyr Leu Ser Ala Ser Tyr
 115 120 125

Gly Asp Ser Leu Val Val Leu Val Ala Thr Val Val Ala Leu Leu Asp
 130 135 140

Ile Cys Phe Ile Leu Val Ala Val Pro Glu Ser Leu Pro Glu Lys Met
 145 150 155 160

Arg Pro Val Ser Trp Gly Ala Gln Ile Ser Trp Lys Gln Ala Asp Pro
 165 170 175

Phe Ala Ser Leu Lys Lys Val Gly Lys Asp Ser Thr Val Leu Leu Ile
 180 185 190

Cys Ile Thr Val Phe Leu Ser Tyr Leu Pro Glu Ala Gly Gln Tyr Ser
 195 200 205

Ser Phe Phe Leu Tyr Leu Arg Gln Val Ile Gly Phe Gly Ser Val Lys
 210 215 220

Ile Ala Ala Phe Ile Ala Met Val Gly Ile Leu Ser Ile Val Ala Gln
 225 230 235 240

Thr Ala Phe Leu Ser Ile Leu Met Arg Ser Leu Gly Asn Lys Asn Thr
 245 250 255

Val Leu Leu Gly Leu Gly Phe Gln Met Leu Gln Leu Ala Trp Tyr Gly
 260 265 270

Phe Gly Ser Gln Ala Trp Met Met Trp Ala Ala Gly Thr Val Ala Ala
 275 280 285

Met Ser Ser Ile Thr Phe Pro Ala Ile Ser Ala Leu Val Ser Arg Asn
 290 295 300

97,

Ala Glu Ser Asp Gln Gln Gly Val Ala Gln Gly Ile Ile Thr Gly Ile
305 310 315 320

Arg Gly Leu Cys Asn Gly Leu Gly Pro Ala Leu Tyr Gly Phe Ile Phe
325 330 335

Tyr Met Phe His Val Glu Leu Thr Glu Leu Gly Pro Lys Leu Asn Ser
340 345 350

Asn Asn Val Pro Leu Gln Gly Ala Val Ile Pro Gly Pro Pro Phe Leu
355 360 365

Phe Gly Ala Cys Ile Val Leu Met Ser Phe Leu Val Ala Leu Phe Ile
370 375 380

Pro Glu Tyr Ser Lys Ala Ser Gly Val Gln Lys His Ser Asn Ser Ser
385 390 395 400

Ser Gly Ser Leu Thr Asn Thr Pro Glu Arg Gly Ser Asp Glu Asp Ile
405 410 415

Glu Pro Leu Leu Gln Asp Ser Ser Ile Trp Glu Leu Ser Ser Phe Glu
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Glu Pro Gly Asn Gln Cys Thr Glu Leu Xaa Thr Arg Gln Lys Val Gly
435 440 445

Phe Cys Ile Arg His Leu
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<210> 141

<211> 2481

<212> DNA

<213> Homo sapiens

<400> 141

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<210> 142

<211> 475

<212> PRT

<213> Homo sapiens

<400> 142

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  20             25             30

Trp Glu Val Asp Trp Phe Ser Leu Ala Ser Val Ile Phe Leu Leu Leu
  35             40             45

Phe Ala Pro Phe Ile Val Tyr Tyr Phe Ile Met Ala Cys Asp Gln Tyr
  50             55             60

Ser Cys Ala Leu Thr Gly Pro Val Val Asp Ile Val Thr Gly His Ala
  65             70             75             80

Arg Leu Ser Asp Ile Trp Ala Lys Thr Pro Pro Ile Thr Arg Lys Ala
  85             90             95

Ala Gln Leu Tyr Thr Leu Trp Val Thr Phe Gln Val Leu Leu Tyr Thr
 100             105             110

Ser Leu Pro Asp Phe Cys His Lys Phe Leu Pro Gly Tyr Val Gly Gly
 115             120             125

Ile Gln Glu Gly Ala Val Thr Pro Ala Gly Val Val Asn Lys Tyr Gln
 130             135             140

Ile Asn Gly Leu Gln Ala Trp Leu Leu Thr His Leu Leu Trp Phe Ala
 145             150             155             160

Asn Ala His Leu Leu Ser Trp Phe Ser Pro Thr Ile Ile Phe Asp Asn
 165             170             175

Trp Ile Pro Leu Leu Trp Cys Ala Asn Ile Leu Gly Tyr Ala Val Ser
 180             185             190

Thr Phe Ala Met Val Lys Gly Tyr Phe Phe Pro Thr Ser Ala Arg Asp
 195             200             205

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Cys Lys Phe Thr Gly Asn Phe Phe Tyr Asn Tyr Met Met Gly Ile Glu
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 Gly Arg Pro Gly Ile Val Ala Trp Thr Leu Ile Asn Leu Ser Phe Ala
 245 250 255
 Ala Lys Gln Arg Glu Leu His Ser His Val Thr Asn Ala Met Val Leu
 260 265 270
 Val Asn Val Leu Gln Ala Ile Tyr Val Ile Asp Phe Phe Trp Asn Glu
 275 280 285
 Thr Trp Tyr Leu Lys Thr Ile Asp Ile Cys His Asp His Phe Gly Trp
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 305 310 315 320
 Gln Gly Leu Tyr Leu Val Tyr His Pro Val Gln Leu Ser Thr Pro His
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 Ala Val Gly Val Leu Leu Leu Gly Leu Val Gly Tyr Tyr Ile Phe Arg
 340 345 350
 Val Ala Asn His Gln Lys Asp Leu Phe Arg Arg Thr Asp Gly Arg Cys
 355 360 365
 Leu Ile Trp Gly Arg Lys Pro Lys Val Ile Glu Cys Ser Tyr Thr Ser
 370 375 380
 Ala Asp Gly Gln Arg His His Ser Lys Leu Leu Val Ser Gly Phe Trp
 385 390 395 400
 Gly Val Ala Arg His Phe Asn Tyr Val Gly Asp Leu Met Gly Ser Leu
 405 410 415
 Ala Tyr Cys Leu Ala Cys Gly Gly Gly His Leu Leu Pro Tyr Phe Tyr
 420 425 430
 Ile Ile Tyr Met Ala Ile Leu Leu Thr His Arg Cys Leu Arg Asp Glu
 435 440 445
 His Arg Cys Ala Ser Lys Tyr Gly Arg Asp Trp Glu Arg Tyr Thr Ala
 450 455 460
 Ala Val Pro Tyr Arg Leu Leu Pro Gly Ile Phe
 465 470 475

<210> 143

<211> 1518

<212> DNA

<213> Homo sapiens

<400> 143

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 cttcactca tggctctaac acatttgcac ttcctctcat ctgagagagt acagtcacgg 180

100

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aagccagctt ttctaccac acacgtttag tttgaagagt atctatTTTT ggaggggtct 360
ttgggaggtt gggcaggctt ctttggatcc cagatacatt tagagctttt tgcattaagt 420
gtgaggaaaa taacttctct ttgatgatgt tgatacacca tgtkggcacc ytggggcaca 480
gcgggttagc tggggagatt ccattgagaat gaacccaaac tactcttctt tgctaggggtc 540
ctttaccac acagaggtga gcctttcagg ttcttcattt tgcttagttt cttcccttgt 600
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tgTtagtg ctaagtatta aaattatcca aattaaatcc ttagcagtca gaacacttgc 1380
ttcactagaa tatgccaaact gccaatcatg ttggactgag ctaatttggt cctctttctg 1440
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aaaaaaaaa aaaaaaaaaa 1518

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<210> 144

<211> 55

<212> PRT

<213> Homo sapiens

<400> 144

```

Met Val Leu Thr His Leu His Phe Leu Ser Ser Gln Arg Val Gln Ser
  1                      5                      10                      15

```

```

Arg Gly Arg Ala Cys Ile Gly Ile Gln Val Leu Leu Val Leu Leu Trp
      20                      25                      30

```

```

Ser Trp Ser Asn Ser Val Ser Trp His Arg Thr Arg Leu Gly Leu His
  35                      40                      45

```

```

Cys Ala Val Cys Phe Thr Ala
  50                      55

```

<210> 145

<211> 2097

<212> DNA

<213> Homo sapiens

<400> 145

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cagtccctcc acctcagctt cccaaagctc tgggattata ggcatgagcc actgtacctg 180
tocacctgag aaattttcta agcctggatt cagtcttatg aaatataata ctttgaaatg 240
cacaataact ttgaaaatga aactcattgc ttttcatttc accaggagt actaactata 300
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atcttgataa ctaaattttg ccaatcattc ttcttgacta gtggtcttta tatatacata 420
catatatata tatatatata tatatatata tatgaggaat tttccataag tgacttgaaa 480
aatacagaat gcactccatg gtaggtctgt tcagtgttat caggaatact gtttctcatc 540
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gagcccaaga ttattgagga gttcaaatat gtgaaagcag aaatgcaaaa gcacggagaa 720
gaccccttct gccctttctc catcatcagc aatgccgtct ctaacatcat ttgctccttg 780

```

101,

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ctttattacc ttcccttttg accatttaag gaattaagac aaattgaaaa ggatataacc 960
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gcttccaccg atgggccaat cttctcattt cttagtgcct cagacatccc atatgtaaaa 2040
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<210> 146

<211> 398

<212> PRT

<213> Homo sapiens

<220>

<221> UNSURE

<222> (379)

<400> 146

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Val Leu Ser Gly Ile Leu Phe Leu Ile Phe Leu Ser Trp Cys Pro Phe
  1             5             10             15

Ala Gly Val Val Phe Ala His Tyr Gly Pro Val Trp Arg Gln Gln Arg
  20             25             30

Lys Phe Ser His Ser Thr Leu Arg His Phe Gly Leu Gly Lys Leu Ser
  35             40             45

Leu Glu Pro Lys Ile Ile Glu Glu Phe Lys Tyr Val Lys Ala Glu Met
  50             55             60

Gln Lys His Gly Glu Asp Pro Phe Cys Pro Phe Ser Ile Ile Ser Asn
  65             70             75             80

Ala Val Ser Asn Ile Ile Cys Ser Leu Cys Phe Gly Gln Arg Phe Asp
  85             90             95

Tyr Thr Asn Ser Glu Phe Lys Lys Met Leu Gly Phe Met Ser Arg Gly
 100             105             110

Leu Glu Ile Cys Leu Asn Ser Gln Val Leu Leu Val Asn Ile Cys Pro
 115             120             125

Trp Leu Tyr Tyr Leu Pro Phe Gly Pro Phe Lys Glu Leu Arg Gln Ile
 130             135             140

Glu Lys Asp Ile Thr Ser Phe Leu Lys Lys Ile Ile Lys Asp His Gln
 145             150             155             160

```

102

Glu Ser Leu Asp Arg Glu Asn Pro Gln Asp Phe Ile Asp Met Tyr Leu
 165 170 175
 Leu His Met Glu Glu Glu Arg Lys Asn Asn Ser Asn Ser Ser Phe Asp
 180 185 190
 Glu Glu Tyr Leu Phe Tyr Ile Ile Gly Asp Leu Phe Ile Ala Gly Thr
 195 200 205
 Asp Thr Thr Thr Asn Ser Leu Leu Trp Cys Leu Leu Tyr Met Ser Leu
 210 215 220
 Asn Pro Asp Val Gln Glu Lys Val His Glu Glu Ile Glu Arg Val Ile
 225 230 235 240
 Gly Ala Asn Arg Ala Pro Ser Leu Thr Asp Lys Ala Gln Met Pro Tyr
 245 250 255
 Thr Glu Ala Thr Ile Met Glu Val Gln Arg Leu Thr Val Val Val Pro
 260 265 270
 Leu Ala Ile Pro His Met Thr Ser Glu Asn Thr Val Leu Gln Gly Tyr
 275 280 285
 Thr Ile Pro Lys Gly Thr Leu Ile Leu Pro Asn Leu Trp Ser Val His
 290 295 300
 Arg Asp Pro Ala Ile Trp Glu Lys Pro Glu Asp Phe Tyr Pro Asn Arg
 305 310 315 320
 Phe Leu Asp Asp Gln Gly Gln Leu Ile Lys Lys Glu Thr Phe Ile Pro
 325 330 335
 Phe Gly Ile Gly Lys Arg Val Cys Met Gly Glu Gln Leu Ala Lys Met
 340 345 350
 Glu Leu Phe Leu Met Phe Val Ser Leu Met Gln Ser Phe Ala Phe Ala
 355 360 365
 Leu Pro Glu Asp Ser Lys Lys Pro Leu Leu Xaa Gly Arg Phe Gly Leu
 370 375 380
 Thr Leu Ala Pro His Pro Phe Asn Ile Thr Ile Ser Arg Arg
 385 390 395

<210> 147

<211> 2504

<212> DNA

<213> Homo sapiens

<400> 147

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 cttttcaaga ttggatcaga gctcatctcc atccagtctt gtttctatga aggcttcaat 360
 ctgtttccat gcaaatttgc taatcagagc ccagagctgc tgggtccctc atctccctca 420
 tctattatag attgacttac agcagggaga gaatctcttt agctcattcc taatgggggtt 480
 gggatcacia tatgggtctgg tccaatctgc atcttggtgt gtccaagac cctatctcct 540

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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaa 2504

```

<210> 148

<211> 66

<212> PRT

<213> Homo sapiens

<400> 148

```

Met Glu Arg Glu Pro Leu Cys Leu Trp Gln Tyr His Leu Glu Arg Ser
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```

```

Thr Ser Tyr Leu Gln Ala Phe Ser Pro Gly Leu Leu Ile Val Ser Val
  20           25           30

```

```

Pro Pro Phe Leu Ser Ser Leu Gln Met Pro Ser Arg Gly Tyr Leu Ile
  35           40           45

```

```

Leu Val Leu Phe Leu Cys Gly Phe Leu Gly Ser Arg Asp Leu Glu Phe
  50           55           60

```

```

Pro Phe
  65

```

<210> 149

<211> 928

<212> DNA

<213> Homo sapiens

<400> 149

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acttgggccc aggcattcca gcttatgatt tcagtgaagt atgatcaca cactgaattc 180
caacctaata gatggagaga gactatgtct ctaaaaataa aaaataaaga gattaggaac 240
tgtctgcact aagatgactt tactattcca agaaatcctt gcctaagaaa gtaaagttga 300
aattactttt ttgtcctgga aactttccga tctatgtatc tgtactcata cagcctcatc 360
gggctaaaca gccttctttt cagaacagta gatcactcaa ctgggttttc aagtgaactg 420
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aaacaaagtc aaaagacaac tgacaaccag gttaaaaaca tgctttcaac atatattaca 840
ggaaaagggc taatattcct aatatgtaaa taattgttag aaattaagag atcaagcacc 900
aagcacccat tagaaaaaaa aaaaaaaa

```

<210> 150

<211> 88

<212> PRT

<213> Homo sapiens

<400> 150

```

Met Tyr Leu Tyr Ser Tyr Ser Leu Ile Gly Leu Asn Ser Leu Leu Phe
  1                      5                      10                      15

```

```

Arg Thr Val Asp His Ser Thr Gly Phe Ser Ser Asp Cys Leu Pro Phe
      20                      25                      30

```

```

Lys Ala Gly Phe Ile Gly Leu Ala Ser Leu Tyr Pro Ala Ile Gln Thr
      35                      40                      45

```

```

Leu Pro Tyr Pro Ser Gln Asp Cys Thr Pro His Val Glu Arg His Thr
      50 *                      55                      60

```

```

Leu Glu Pro Asp Ser Pro Lys Leu Thr Asn Ile Pro Pro Leu Thr Pro
      65                      70                      75                      80

```

```

Phe Ser Glu Ala Thr Lys Ile Met
      85

```

<210> 151

<211> 1343

<212> DNA

<213> Homo sapiens

<400> 151

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ggggagtgtt tgcgtttctt ctccgtttgg cagtgaacaa catctcagaa aggtggagct 180
gatcagaata atgttcagca tcaacccctt ggagaacctg aaggtgtaca tcagcagtcg 240
gcctcccttg gtggtcttca tgatcagcgt aagcgccatg gccatagctt tctgacctc 300
gggctacttc ttcaaaatca aggagattaa atccccagaa atggcagagg attggaatac 360
ttttctgcta cggttcaatg atttggaact gtgtgtatca gagaatgaaa cctcaagca 420
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caccagtc cccagggccc tggaggactc gggcccgggtg aatatctcag tctcaatcac 540
cctaaccctg gaccactga aacccttcgg agggatttcc cgcaacgtca cccatctgta 600
ctcaaccatc ttagggcac agattggact ttcaggcagg gaagcccacg aggagataaa 660
catcaccttc accctgccta cagcgtggag ctcagatgac tgcgcctcc acggtcactg 720
tgagcaggtg gtattcacag cctgcatgac cctcacggcc agccctgggg tgttccccgt 780
cactgtacag ccaccgcact gtgttctga cacgtacagc aacgccacgc tctggtacaa 840

```

105.

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<210> 152

<211> 314

<212> PRT

<213> Homo sapiens

<400> 152

Met Phe Ser Ile Asn Pro Leu Glu Asn Leu Lys Val Tyr Ile Ser Ser
 1 5 10 15

Arg Pro Pro Leu Val Val Phe Met Ile Ser Val Ser Ala Met Ala Ile
 20 25 30

Ala Phe Leu Thr Leu Gly Tyr Phe Phe Lys Ile Lys Glu Ile Lys Ser
 35 40 45

Pro Glu Met Ala Glu Asp Trp Asn Thr Phe Leu Leu Arg Phe Asn Asp
 50 55 60

Leu Asp Leu Cys Val Ser Glu Asn Glu Thr Leu Lys His Leu Thr Asn
 65 70 75 80

Asp Thr Thr Thr Pro Glu Ser Thr Met Thr Ser Gly Gln Ala Arg Ala
 85 90 95

Ser Thr Gln Ser Pro Gln Ala Leu Glu Asp Ser Gly Pro Val Asn Ile
 100 105 110

Ser Val Ser Ile Thr Leu Thr Leu Asp Pro Leu Lys Pro Phe Gly Gly
 115 120 125

Tyr Ser Arg Asn Val Thr His Leu Tyr Ser Thr Ile Leu Gly His Gln
 130 135 140

Ile Gly Leu Ser Gly Arg Glu Ala His Glu Glu Ile Asn Ile Thr Phe
 145 150 155 160

Thr Leu Pro Thr Ala Trp Ser Ser Asp Asp Cys Ala Leu His Gly His
 165 170 175

Cys Glu Gln Val Val Phe Thr Ala Cys Met Thr Leu Thr Ala Ser Pro
 180 185 190

Gly Val Phe Pro Val Thr Val Gln Pro Pro His Cys Val Pro Asp Thr
 195 200 205

Tyr Ser Asn Ala Thr Leu Trp Tyr Lys Ile Phe Thr Thr Ala Arg Asp
 210 215 220

Ala Asn Thr Lys Tyr Ala Gln Asp Tyr Asn Pro Phe Trp Cys Tyr Lys
 225 230 235 240

106,

Gly Ala Ile Gly Lys Val Tyr His Ala Leu Asn Pro Lys Leu Thr Val
 245 250 255

Ile Val Pro Asp Asp Asp Arg Ser Leu Ile Asn Leu His Leu Met His
 260 265 270

Thr Ser Tyr Phe Leu Phe Val Met Val Ile Thr Met Phe Cys Tyr Ala
 275 280 285

Val Ile Lys Gly Arg Pro Ser Lys Leu Arg Gln Ser Asn Pro Glu Phe
 290 295 300

Cys Pro Glu Lys Val Ala Leu Ala Glu Ala
 305 310

<210> 153

<211> 3343

<212> DNA

<213> Homo sapiens

<400> 153

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107.

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<210> 154

<211> 389

<212> PRT

<213> Homo sapiens

<400> 154

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Met Trp Ile Lys Phe Ser Ser Asp Glu Glu Leu Glu Gly Leu Gly Phe
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Arg Ala Lys Tyr Ser Phe Ile Pro Asp Pro Asp Phe Thr Tyr Leu Gly
      20             25             30

Gly Ile Leu Asn Pro Ile Pro Asp Cys Gln Phe Glu Leu Ser Gly Ala
      35             40             45

Asp Gly Ile Val Arg Ser Ser Gln Val Glu Gln Glu Glu Lys Thr Lys
      50             55             60

Pro Gly Gln Ala Val Asp Cys Ile Trp Thr Ile Lys Ala Thr Pro Lys
      65             70             75             80

Ala Lys Ile Tyr Leu Arg Phe Leu Asp Tyr Gln Met Glu His Ser Asn
      85             90             95

Glu Cys Lys Arg Asn Phe Val Ala Val Tyr Asp Gly Ser Ser Ser Ile
      100            105            110

Glu Asn Leu Lys Ala Lys Phe Cys Ser Thr Val Ala Asn Asp Val Met
      115            120            125

Leu Lys Thr Gly Ile Gly Val Ile Arg Met Trp Ala Asp Glu Gly Ser
      130            135            140

Arg Leu Ser Arg Phe Arg Met Leu Phe Thr Ser Phe Val Glu Pro Pro
      145            150            155            160

Cys Thr Ser Ser Thr Phe Phe Cys His Ser Asn Met Cys Ile Asn Asn
      165            170            175

Ser Leu Val Cys Asn Gly Val Gln Asn Cys Ala Tyr Pro Trp Asp Glu
      180            185            190

Asn His Cys Lys Glu Lys Lys Lys Ala Gly Val Phe Glu Gln Ile Thr
      195            200            205

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108,

Lys Thr His Gly Thr Ile Ile Gly Ile Thr Ser Gly Ile Val Leu Val
 210 215 220
 Leu Leu Ile Ile Ser Ile Leu Val Gln Val Lys Gln Pro Arg Lys Lys
 225 230 235 240
 Val Met Ala Cys Lys Thr Ala Phe Asn Lys Thr Gly Phe Gln Glu Val
 245 250 255
 Phe Asp Pro Pro His Tyr Glu Leu Phe Ser Leu Arg Asp Lys Glu Ile
 260 265 270
 Ser Ala Asp Leu Ala Asp Leu Ser Glu Glu Leu Asp Asn Tyr Gln Lys
 275 280 285
 Met Arg Arg Ser Ser Thr Ala Ser Arg Cys Ile His Asp His His Cys
 290 295 300
 Gly Ser Gln Ala Ser Ser Val Lys Gln Ser Arg Thr Asn Leu Ser Ser
 305 310 315 320
 Met Glu Leu Pro Phe Arg Asn Asp Phe Ala Gln Pro Gln Pro Met Lys
 325 330 335
 Thr Phe Asn Ser Thr Phe Lys Lys Ser Ser Tyr Thr Phe Lys Gln Gly
 340 345 350
 His Glu Cys Pro Glu Gln Ala Leu Glu Asp Arg Val Met Glu Glu Ile
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 Pro Cys Glu Ile Tyr Val Arg Gly Arg Glu Asp Ser Ala Gln Ala Ser
 370 375 380
 Ile Ser Ile Asp Phe
 385

<210> 155
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 <212> DNA
 <213> Homo sapiens

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 <222> (1270)

<220>
 <221> unsure
 <222> (2613)

<400> 155

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<210> 156

<211> 95

<212> PRT

<213> Homo sapiens

<400> 156

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Met Asp Phe Ala Ala Ser Ile Glu Ala Met Trp Leu His Cys Leu Pro
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Ile Ser Gln Thr Val Leu Ser Gly Gly Pro Ser Ile Thr Ser Met Gln
  20                      25                      30

```

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Val Glu Gly Lys Asn Ser Ile Ile Leu Thr Phe Arg Gln Leu Met Ala
  35                      40                      45

```

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Glu Glu Gly Pro Trp Gly Leu Met Lys Gly Leu Ser Ala Arg Ile Ile
  50                      55                      60

```

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Ser Ala Thr Pro Ser Thr Ile Val Ile Val Val Gly Tyr Glu Ser Leu
  65                      70                      75                      80

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110.

Lys Lys Leu Ser Leu Arg Pro Glu Leu Val Asp Ser Arg His Trp
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<210> 157
 <211> 2293
 <212> DNA
 <213> Homo sapiens

<400> 157
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<210> 158
 <211> 586
 <212> PRT
 <213> Homo sapiens

<220>
 <221> UNSURE
 <222> (286)

<400> 158
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111,

Cys Ser Gly His Cys Gly Gly His Cys Ser Gly Pro Leu Leu Pro Pro
 20 25 30
 Pro Ser Ser Gln Pro Leu Pro Ser Thr His Arg Asp Pro Gly Cys Lys
 35 40 45
 Gly His Lys Phe Ala His Ser Gly Leu Ala Cys Gln Leu Pro Gln Pro
 50 55 60
 Cys Glu Ala Asp Glu Gly Leu Gly Glu Glu Asp Ser Ser Ser Glu
 65 70 75 80
 Arg Ser Ser Cys Thr Ser Ser Ser Thr His Gln Arg Asp Gly Lys Phe
 85 90 95
 Cys Asp Cys Cys Tyr Cys Glu Phe Phe Gly His Asn Ala Pro Pro Ala
 100 105 110
 Ala Pro Thr Ser Arg Asn Tyr Thr Glu Ile Arg Glu Lys Leu Arg Ser
 115 120 125
 Arg Leu Thr Arg Arg Lys Glu Glu Leu Pro Met Lys Gly Gly Thr Leu
 130 135 140
 Gly Gly Ile Pro Gly Glu Pro Ala Val Asp His Arg Asp Val Asp Glu
 145 150 155 160
 Leu Leu Glu Phe Ile Asn Ser Thr Glu Pro Lys Val Pro Asn Ser Ala
 165 170 175
 Arg Ala Ala Lys Arg Ala Arg His Lys Leu Lys Lys Lys Glu Lys Glu
 180 185 190
 Lys Ala Gln Leu Ala Ala Glu Ala Leu Lys Gln Ala Asn Arg Val Ser
 195 200 205
 Gly Ser Arg Glu Pro Arg Pro Ala Arg Glu Arg Leu Leu Glu Trp Pro
 210 215 220
 Asp Arg Glu Leu Asp Arg Val Asn Ser Phe Leu Ser Ser Arg Leu Gln
 225 230 235 240
 Glu Ile Lys Asn Thr Val Lys Asp Ser Ile Arg Ala Ser Phe Ser Val
 245 250 255
 Cys Glu Leu Ser Met Asp Ser Asn Gly Phe Ser Lys Glu Gly Ala Ala
 260 265 270
 Glu Pro Glu Pro Gln Ser Leu Pro Pro Ser Asn Leu Ser Xaa Ser Ser
 275 280 285
 Glu Gln Gln Pro Asp Ile Asn Leu Asp Leu Ser Pro Leu Thr Leu Gly
 290 295 300
 Ser Pro Gln Asn His Thr Leu Gln Ala Pro Gly Glu Pro Ala Pro Pro
 305 310 315 320
 Trp Ala Glu Met Arg Gly Pro His Pro Pro Trp Thr Glu Val Arg Gly
 325 330 335

112

Pro Pro Pro Gly Ile Val Pro Glu Asn Gly Leu Val Arg Arg Leu Asn
 340 345 350
 Thr Val Pro Asn Leu Ser Arg Val Ile Trp Val Lys Thr Pro Lys Pro
 355 360 365
 Gly Tyr Pro Ser Ser Glu Glu Pro Ser Ser Lys Glu Val Pro Ser Cys
 370 375 380
 Lys Gln Glu Leu Pro Glu Pro Val Ser Ser Gly Gly Lys Pro Gln Lys
 385 390 395 400
 Gly Lys Arg Gln Gly Ser Gln Ala Lys Lys Ser Glu Ala Ser Pro Ala
 405 410 415
 Pro Arg Pro Pro Ala Ser Leu Glu Val Pro Ser Ala Lys Gly Gln Val
 420 425 430
 Ala Gly Pro Lys Gln Pro Gly Arg Val Leu Glu Leu Pro Lys Val Gly
 435 440 445
 Ser Cys Ala Glu Ala Gly Glu Gly Ser Arg Gly Ser Arg Pro Gly Pro
 450 455 460
 Gly Trp Ala Gly Ser Pro Lys Thr Glu Lys Glu Lys Gly Ser Ser Trp
 465 470 475 480
 Arg Asn Trp Pro Gly Glu Ala Lys Ala Arg Pro Gln Glu Gln Glu Ser
 485 490 495
 Val Gln Pro Pro Gly Pro Ala Arg Pro Gln Ser Leu Pro Gln Gly Lys
 500 505 510
 Gly Arg Ser Arg Arg Ser Arg Asn Lys Gln Glu Lys Pro Ala Ser Ser
 515 520 525
 Leu Asp Asp Val Phe Leu Pro Lys Asp Met Asp Gly Val Glu Met Asp
 530 535 540
 Glu Thr Asp Arg Glu Val Glu Tyr Phe Lys Arg Phe Cys Leu Asp Ser
 545 550 555 560
 Ala Lys Gln Thr Arg Gln Lys Val Ala Val Asn Trp Thr Asn Phe Ser
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 Leu Lys Lys Thr Thr Pro Ser Thr Ala Gln
 580 585

<210> 159

<211> 1704

<212> DNA

<213> Homo sapiens

<400> 159

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 ttccacaaac atgtggagtt tgatttcctt attaagggcc agtttctgcg aatgcccttg 360
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113.

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<210> 160

<211> 423

<212> PRT

<213> Homo sapiens

<400> 160

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Val Asp Asp Val Pro Phe Ser Ile Pro Ala Ala Ser Glu Ile Ala Asp
      20                      25                      30

Leu Ser Asn Ile Ile Asn Lys Leu Leu Lys Asp Lys Asn Glu Phe His
      35                      40                      45

Lys His Val Glu Phe Asp Phe Leu Ile Lys Gly Gln Phe Leu Arg Met
      50                      55                      60

Pro Leu Asp Lys His Met Glu Met Glu Asn Ile Ser Ser Glu Glu Val
      65                      70                      75                      80

Val Glu Ile Glu Tyr Val Glu Lys Tyr Thr Ala Pro Gln Pro Glu Gln
      85                      90                      95

Cys Met Phe His Asp Asp Trp Ile Ser Ser Ile Lys Gly Ala Glu Glu
      100                      105                      110

Trp Ile Leu Thr Gly Ser Tyr Asp Lys Thr Ser Arg Ile Trp Ser Leu
      115                      120                      125

Glu Gly Lys Ser Ile Met Thr Ile Val Gly His Thr Asp Val Val Lys
      130                      135                      140

Asp Val Ala Trp Val Lys Lys Asp Ser Leu Ser Cys Leu Leu Leu Ser
      145                      150                      155                      160

Ala Ser Met Asp Gln Thr Ile Leu Leu Trp Glu Trp Asn Val Glu Arg
      165                      170                      175

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114

Asn Lys Val Lys Ala Leu His Cys Cys Arg Gly His Ala Gly Ser Val
 180 185 190
 Asp Ser Ile Ala Val Asp Gly Ser Gly Thr Lys Phe Cys Ser Gly Ser
 195 200 205
 Trp Asp Lys Met Leu Lys Ile Trp Ser Thr Val Pro Thr Asp Glu Glu
 210 215 220
 Asp Glu Met Glu Glu Ser Thr Asn Arg Pro Arg Lys Lys Gln Lys Thr
 225 230 235 240
 Glu Gln Leu Gly Leu Thr Arg Thr Pro Ile Val Thr Leu Ser Gly His
 245 250 255
 Met Glu Ala Val Ser Ser Val Leu Trp Ser Asp Ala Glu Glu Ile Cys
 260 265 270
 Ser Ala Ser Trp Asp His Thr Ile Arg Val Trp Asp Val Glu Ser Gly
 275 280 285
 Ser Leu Lys Ser Thr Leu Thr Gly Asn Lys Val Phe Asn Cys Ile Ser
 290 295 300
 Tyr Ser Pro Leu Cys Lys Arg Leu Ala Ser Gly Ser Thr Asp Arg His
 305 310 315 320
 Ile Arg Leu Trp Asp Pro Arg Thr Lys Asp Gly Ser Leu Val Ser Leu
 325 330 335
 Ser Leu Thr Ser His Thr Gly Trp Val Thr Ser Val Lys Trp Ser Pro
 340 345 350
 Thr His Glu Gln Gln Leu Ile Ser Gly Ser Leu Asp Asn Ile Val Lys
 355 360 365
 Leu Trp Asp Thr Arg Ser Cys Lys Ala Pro Leu Tyr Asp Leu Ala Ala
 370 375 380
 His Glu Asp Lys Val Leu Ser Val Asp Trp Thr Asp Thr Gly Leu Leu
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 Leu Ser Gly Gly Ala Asp Asn Lys Leu Tyr Ser Tyr Arg Tyr Ser Pro
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 Thr Thr Ser His Val Gly Ala
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<210> 161

<211> 2302

<212> DNA

<213> Homo sapiens

<400> 161

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 tttattgggg tgggggggta attttgcctt accctgttca ctttcagatg awtaggcttt 420

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ttaaaaaaaa aaaaaaaaaa aa 2302

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<210> 162

<211> 94

<212> PRT

<213> Homo sapiens

<400> 162

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Met Pro Glu Cys Ile Phe Val Leu Leu Gly Pro Trp Asn Arg Tyr Arg
 1             5             10             15

```

```

Cys Phe Leu Lys Asp Glu Arg Asn Ala Met Gly Ala Leu His Ala Arg
 20             25             30

```

```

Leu Gln Thr Tyr Gln Glu Cys Ile Ile Val Ser Leu Phe Pro Asn Lys
 35             40             45

```

```

Glu Met Arg Val Thr Ser Phe Gly Leu Leu Thr Leu Met Gly Val Ala
 50             55             60

```

```

Cys Leu Leu Leu Leu Ile Ile Val Ser Cys Ser Asp Met Ile His Ser
 65             70             75             80

```

```

Pro Ala Phe Thr Ala Phe His Leu Met Ile Leu Asp Arg Phe
 85             90

```

<210> 163

<211> 1538

<212> DNA

<213> Homo sapiens

116.

<400> 163

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<210> 164

<211> 415

<212> PRT

<213> Homo sapiens

<220>

<221> UNSURE

<222> (20)

<220>

<221> UNSURE

<222> (65)

<400> 164

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Met Asn Phe Ser Glu Val Phe Lys Leu Ser Ser Leu Leu Cys Lys Phe
  1                      5                      10          15

Ser Pro Asp Xaa Lys Tyr Leu Ala Ser Cys Val Gln Tyr Arg Leu Val
      20                      25                      30

Val Arg Asp Val Asn Thr Leu Gln Ile Leu Gln Leu Tyr Thr Cys Leu
      35                      40                      45

Asp Gln Ile Gln His Ile Glu Trp Ser Ala Asp Ser Leu Phe Ile Leu
      50                      55                      60

Xaa Ala Met Tyr Lys Arg Gly Leu Val Gln Val Trp Ser Leu Glu Gln
      65                      70                      75          80

Pro Glu Trp His Cys Lys Ile Asp Glu Gly Ser Ala Gly Leu Val Ala
      85                      90                      95

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117

Ser Cys Trp Ser Pro Asp Gly Arg His Ile Leu Asn Thr Thr Glu Phe
 100 105 110
 His Leu Arg Ile Thr Val Trp Ser Leu Cys Thr Lys Ser Val Ser Tyr
 115 120 125
 Ile Lys Tyr Pro Lys Ala Cys Leu Gln Gly Ile Thr Phe Thr Arg Asp
 130 135 140
 Gly Arg Tyr Met Ala Leu Ala Glu Arg Arg Asp Cys Lys Asp Tyr Val
 145 150 155 160
 Ser Ile Phe Val Cys Ser Asp Trp Gln Leu Leu Arg His Phe Asp Thr
 165 170 175
 Asp Thr Gln Asp Leu Thr Gly Ile Glu Trp Ala Pro Asn Gly Cys Val
 180 185 190
 Leu Ala Val Trp Asp Thr Cys Leu Glu Val Arg Ile Leu Asn His Val
 195 200 205
 Thr Trp Lys Met Ile Thr Glu Phe Gly His Pro Ala Ala Ile Asn Asp
 210 215 220
 Pro Lys Ile Val Val Tyr Lys Glu Ala Glu Lys Ser Pro Gln Leu Gly
 225 230 235 240
 Leu Gly Cys Leu Ser Phe Pro Pro Pro Arg Ala Gly Ala Gly Pro Leu
 245 250 255
 Pro Ser Ser Glu Ser Lys Tyr Glu Ile Ala Ser Val Pro Val Ser Leu
 260 265 270
 Gln Thr Leu Lys Pro Val Thr Asp Arg Ala Asn Pro Lys Met Gly Ile
 275 280 285
 Gly Met Leu Ala Phe Ser Pro Asp Ser Tyr Phe Leu Ala Thr Arg Asn
 290 295 300
 Asp Asn Ile Pro Asn Ala Val Trp Val Trp Asp Ile Gln Lys Leu Arg
 305 310 315 320
 Leu Phe Ala Val Leu Glu Gln Leu Ser Pro Val Arg Ala Phe Gln Trp
 325 330 335
 Asp Pro Gln Gln Pro Arg Leu Ala Ile Cys Thr Gly Gly Ser Arg Leu
 340 345 350
 Tyr Leu Trp Ser Pro Ala Gly Cys Met Ser Val Gln Val Pro Gly Glu
 355 360 365
 Gly Asp Phe Ala Val Leu Ser Leu Cys Trp His Leu Ser Gly Asp Ser
 370 375 380
 Met Ala Leu Leu Ser Lys Asp His Phe Cys Leu Cys Phe Leu Glu Thr
 385 390 395 400
 Glu Ala Val Val Gly Thr Ala Cys Arg Gln Leu Gly Gly His Thr
 405 410 415

<210> 165

<211> 3178
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (1653)

<220>
<221> unsure
<222> (1767)

<400> 165
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tgagaatggt cattatgact tagagaatgc tacacgtgta ggttgctggt gtgtcctgaa 360
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119.

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<210> 166

<211> 67

<212> PRT

<213> Homo sapiens

<400> 166

Met Ile Asn Thr Phe Thr Tyr Met Val Val Cys Leu Ser Glu Leu Phe
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Ser Pro Ile Tyr Ser Pro Ser Val Tyr Gly Ser Val His Phe Cys His
 20 25 30

Thr Pro Gly Asn Pro Val Ile Leu Phe Leu Asn Ile Leu Leu Met Asp
 35 40 45

Leu Cys Ser Cys Leu Asn Val Phe Asn Phe Gln Gln Asn Glu Pro His
 50 55 60

Ser Leu Phe

65

<210> 167

<211> 2401

<212> DNA

<213> Homo sapiens

<400> 167

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120.

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<210> 168

<211> 498

<212> PRT

<213> Homo sapiens

<400> 168

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Met Gln Glu Ser Gly Cys Arg Leu Glu His Pro Ser Ala Thr Lys Phe
  1              5              10              15

```

```

Arg Asn His Val Met Glu Gly Asp Trp Asp Lys Ala Glu Asn Asp Leu
      20              25              30

```

```

Asn Glu Leu Lys Pro Leu Val His Ser Pro His Ala Ile Val Arg Met
  35              40              45

```

```

Lys Phe Leu Leu Leu Gln Gln Lys Tyr Leu Glu Tyr Leu Glu Asp Gly
  50              55              60

```

```

Lys Val Leu Glu Ala Leu Gln Val Leu Arg Cys Glu Leu Thr Pro Leu
  65              70              75              80

```

```

Lys Tyr Asn Thr Glu Arg Ile His Val Leu Ser Gly Tyr Leu Met Cys
      85              90              95

```

```

Ser His Ala Glu Asp Leu Arg Ala Lys Ala Glu Trp Glu Gly Lys Gly
    100              105              110

```

```

Thr Ala Ser Arg Ser Lys Leu Leu Asp Lys Leu Gln Thr Tyr Leu Pro
    115              120              125

```

```

Pro Ser Val Met Leu Pro Pro Arg Arg Leu Gln Thr Leu Leu Arg Gln
    130              135              140

```

```

Ala Val Glu Leu Gln Arg Asp Arg Cys Leu Tyr His Asn Thr Lys Leu
    145              150              155              160

```

```

Asp Asn Asn Leu Asp Ser Val Ser Leu Leu Ile Asp His Val Cys Ser
    165              170              175

```

```

Arg Arg Gln Phe Pro Cys Tyr Thr Gln Gln Ile Leu Thr Glu His Cys
    180              185              190

```

```

Asn Glu Val Trp Phe Cys Lys Phe Ser Asn Asp Gly Thr Lys Leu Ala
    195              200              205

```

```

Thr Gly Ser Lys Asp Thr Val Ile Ile Trp Gln Val Asp Pro Asp
    210              215              220

```

121

Thr His Leu Leu Lys Leu Leu Lys Thr Leu Glu Gly His Ala Tyr Gly
 225 230 235 240
 Val Ser Tyr Ile Ala Trp Ser Pro Asp Asp Asn Tyr Leu Val Ala Cys
 245 250 255
 Gly Pro Asp Asp Cys Ser Glu Leu Trp Leu Trp Asn Val Gln Thr Gly
 260 265 270
 Glu Leu Arg Thr Lys Met Ser Gln Ser His Glu Asp Ser Leu Thr Ser
 275 280 285
 Val Ala Trp Asn Pro Asp Gly Lys Arg Phe Val Thr Gly Gly Gln Arg
 290 295 300
 Gly Gln Phe Tyr Gln Cys Asp Leu Asp Gly Asn Leu Leu Asp Ser Trp
 305 310 315 320
 Glu Gly Val Arg Val Gln Cys Leu Trp Cys Leu Ser Asp Gly Lys Thr
 325 330 335
 Val Leu Ala Ser Asp Thr His Gln Arg Ile Arg Gly Tyr Asn Phe Glu
 340 345 350
 Asp Leu Thr Asp Arg Asn Ile Val Gln Glu Asp His Pro Ile Met Ser
 355 360 365
 Phe Thr Ile Ser Lys Asn Gly Arg Leu Ala Leu Leu Asn Val Ala Thr
 370 375 380
 Gln Gly Val His Leu Trp Asp Leu Gln Asp Arg Val Leu Val Arg Lys
 385 390 395 400
 Tyr Gln Gly Val Thr Gln Gly Phe Tyr Thr Ile His Ser Cys Phe Gly
 405 410 415
 Gly His Asn Glu Asp Phe Ile Ala Ser Gly Ser Glu Asp His Lys Val
 420 425 430
 Tyr Ile Trp His Lys Arg Ser Glu Leu Pro Ile Ala Glu Leu Thr Gly
 435 440 445
 His Thr Arg Thr Val Asn Cys Val Ser Trp Asn Pro Gln Ile Pro Ser
 450 455 460
 Met Met Ala Ser Ala Ser Asp Asp Gly Thr Val Arg Ile Trp Gly Pro
 465 470 475 480
 Ala Pro Phe Ile Asp His Gln Asn Ile Glu Glu Glu Cys Ser Ser Met
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Asp Ser

<210> 169

<211> 1110

<212> DNA

<213> Homo sapiens

<400> 169

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122,

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ctcactgaca gaattaaaaa aaaaaaaaaa 1110

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<210> 170

<211> 193

<212> PRT

<213> Homo sapiens

<400> 170

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Tyr Phe Ile Phe Gly Phe Asn Val Ile Phe Trp Phe Leu Gly Ile Thr
  20              25              30

Phe Leu Gly Ile Gly Leu Trp Ala Trp Asn Glu Lys Gly Val Leu Ser
  35              40              45

Asn Ile Ser Ser Ile Thr Asp Leu Gly Gly Phe Asp Pro Val Trp Leu
  50              55              60

Phe Leu Val Val Gly Gly Val Met Phe Ile Leu Gly Phe Ala Gly Cys
  65              70              75              80

Ile Gly Ala Leu Arg Glu Asn Thr Phe Leu Leu Lys Phe Phe Ser Val
  85              90              95

Phe Leu Gly Ile Ile Phe Phe Leu Glu Leu Thr Ala Gly Val Leu Ala
 100              105              110

Phe Val Phe Lys Asp Trp Ile Lys Asp Gln Leu Tyr Phe Phe Ile Asn
 115              120              125

Asn Asn Ile Arg Ala Tyr Arg Asp Asp Ile Asp Leu Gln Asn Leu Ile
 130              135              140

Asp Phe Thr Gln Glu Tyr Ile Pro Met Gln Val Glu Ser Asp Val Ala
 145              150              155              160

Phe His Ser Pro Ala Ala Leu Lys Ile Pro Gln Lys Met Ser Ser Thr
 165              170              175

Leu Ser Val Ala Met Met Pro Gly Lys Asn Gln Lys Leu Thr Ser Arg
 180              185              190

Leu

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<210> 171
 <211> 1621
 <212> DNA
 <213> Homo sapiens

<400> 171
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 aaggtctgct aggcagcttc acagcctttt ctttcctctt ctctatcaga ggtctctttg 180
 gaagcaataa tgatgactat aacaagaact tatcttgctt tgcaagattc ttccgccgtc 240
 agagtttctg atttatcttc tgggggttcca tgtatgccag ggagaaagag agagcgcgaa 300
 agagagagga tgtctctctc agactggcac ctggcggtga agctggctga ccagccactt 360
 actccaaagt ctattcttcg gttgccagag acagaactgg gagaatactc gctagggggc 420
 tatagtattt catttctgaa gcagcttatt gctggcaaac tccaggagtc tgttccagac 480
 cctgagctga ttgatctgat ctactgtggt cggaagctaa aagatgacca gacacttgac 540
 ttctatggga ttcaacctgg gtccactgtc catgttctgc gaaagtctg gcctgaacct 600
 gatcagaac cggaacctgt ggacaaagt gctgccatga gagagttccg ggtgttgac 660
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 ggcagtgcct caatgcctgg gactgactcc tcttcccgga gcatgccctc cagctcatac 960
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 ggagccccat gaactccctg cttcccctga acccccagca agttgcagag gctactgccc 1500
 ttgggaggga ctcataaagg tgccctccatc tctcccttcc ccaatatacc tgatgggtcaa 1560
 ctctaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1620
 a 1621

<210> 172
 <211> 420
 <212> PRT
 <213> Homo sapiens

<400> 172
 Met Met Thr Ile Thr Arg Thr Tyr Leu Ala Leu Gln Asp Ser Ser Ala
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 Val Arg Val Ser Asp Leu Phe Ser Gly Val Pro Cys Met Pro Gly Arg
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 Lys Arg Glu Arg Glu Arg Glu Arg Met Ser Leu Ser Asp Trp His Leu
 35 40 45
 Ala Val Lys Leu Ala Asp Gln Pro Leu Thr Pro Lys Ser Ile Leu Arg
 50 55 60
 Leu Pro Glu Thr Glu Leu Gly Glu Tyr Ser Leu Gly Gly Tyr Ser Ile
 65 70 75 80
 Ser Phe Leu Lys Gln Leu Ile Ala Gly Lys Leu Gln Glu Ser Val Pro
 85 90 95

124

Asp Pro Glu Leu Ile Asp Leu Ile Tyr Cys Gly Arg Lys Leu Lys Asp
 100 105 110
 Asp Gln Thr Leu Asp Phe Tyr Gly Ile Gln Pro Gly Ser Thr Val His
 115 120 125
 Val Leu Arg Lys Ser Trp Pro Glu Pro Asp Gln Lys Pro Glu Pro Val
 130 135 140
 Asp Lys Val Ala Ala Met Arg Glu Phe Arg Val Leu His Thr Ala Leu
 145 150 155 160
 His Ser Ser Ser Ser Tyr Arg Glu Ala Val Phe Lys Met Leu Ser Asn
 165 170 175
 Lys Glu Ser Leu Asp Gln Ile Ile Val Ala Thr Pro Gly Leu Ser Ser
 180 185 190
 Asp Pro Ile Ala Leu Gly Val Leu Gln Asp Lys Asp Leu Phe Ser Val
 195 200 205
 Phe Ala Asp Pro Asn Met Leu Asp Thr Leu Val Pro Ala His Pro Ala
 210 215 220
 Leu Val Asn Ala Ile Val Leu Val Leu His Ser Val Ala Gly Ser Ala
 225 230 235 240
 Pro Met Pro Gly Thr Asp Ser Ser Ser Arg Ser Met Pro Ser Ser Ser
 245 250 255
 Tyr Arg Asp Met Pro Gly Gly Phe Leu Phe Glu Gly Leu Ser Asp Asp
 260 265 270
 Glu Asp Asp Phe His Pro Asn Thr Arg Ser Thr Pro Ser Ser Ser Thr
 275 280 285
 Pro Ser Ser Arg Pro Ala Ser Leu Gly Tyr Ser Gly Ala Ala Gly Pro
 290 295 300
 Arg Pro Ile Thr Gln Ser Glu Leu Ala Thr Ala Leu Ala Leu Ala Ser
 305 310 315 320
 Thr Pro Glu Ser Ser Ser His Thr Pro Thr Pro Gly Thr Gln Gly His
 325 330 335
 Ser Ser Gly Thr Ser Pro Met Ser Ser Gly Val Gln Ser Gly Thr Pro
 340 345 350
 Ile Thr Asn Asp Leu Phe Ser Gln Ala Leu Gln His Ala Leu Gln Ala
 355 360 365
 Ser Gly Gln Pro Ser Leu Gln Ser Gln Trp Gln Pro Gln Leu Gln Gln
 370 375 380
 Leu Arg Asp Met Gly Ile Gln Asp Asp Glu Leu Ser Leu Arg Ala Leu
 385 390 395 400
 Gln Ala Thr Gly Gly Asp Ile Gln Ala Ala Leu Glu Leu Ile Phe Ala
 405 410 415
 Gly Gly Ala Pro
 420

125

<210> 173
 <211> 1534
 <212> DNA
 <213> Homo sapiens

<400> 173
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 gacccatcct ttctcgtcgg aataccgtct ggctgtgcta cgaagtgaaa acaaaggggtc 180
 cctcaaggcc ccctttggac gcaaagatct ttcgaggcca ggtgtattcc gaacttaagt 240
 accaccaga gatgagattc ttccactggt tcagcaagtg gaggaagctg catcgtgacc 300
 aggagtatga ggtcacctgg tacatatcct ggagcccctg cacaagtgt acaagggata 360
 tggccacgtt cctggccgag gaccogaagg ttaccctgac catcttcgtt gccgcctct 420
 actacttctg ggaccagat taccaggagg cgcttcgag cctgtgtcag aaaagagacg 480
 gtccgcgtgc caccatgaag atcatgaatt atgacgaatt tcagcactgt tggagcaagt 540
 tcgtgtacag ccaaagagag ctatttgagc cttggaataa tctgcctaaa tattatata 600
 tactgcacat catgctgggg gagattctca gacactcgat ggatccaccc acattcactt 660
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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1500
 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaa 1534

<210> 174
 <211> 384
 <212> PRT
 <213> Homo sapiens

<400> 174
 Met Lys Pro His Phe Arg Asn Thr Val Glu Arg Met Tyr Arg Asp Thr
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 Phe Ser Tyr Asn Phe Tyr Asn Arg Pro Ile Leu Ser Arg Arg Asn Thr
 20 25 30
 Val Trp Leu Cys Tyr Glu Val Lys Thr Lys Gly Pro Ser Arg Pro Pro
 35 40 45
 Leu Asp Ala Lys Ile Phe Arg Gly Gln Val Tyr Ser Glu Leu Lys Tyr
 50 55 60
 His Pro Glu Met Arg Phe Phe His Trp Phe Ser Lys Trp Arg Lys Leu
 65 70 75 80
 His Arg Asp Gln Glu Tyr Glu Val Thr Trp Tyr Ile Ser Trp Ser Pro
 85 90 95
 Cys Thr Lys Cys Thr Arg Asp Met Ala Thr Phe Leu Ala Glu Asp Pro
 100 105 110

126

Lys Val Thr Leu Thr Ile Phe Val Ala Arg Leu Tyr Tyr Phe Trp Asp
 115 120 125
 Pro Asp Tyr Gln Glu Ala Leu Arg Ser Leu Cys Gln Lys Arg Asp Gly
 130 135 140
 Pro Arg Ala Thr Met Lys Ile Met Asn Tyr Asp Glu Phe Gln His Cys
 145 150 155 160
 Trp Ser Lys Phe Val Tyr Ser Gln Arg Glu Leu Phe Glu Pro Trp Asn
 165 170 175
 Asn Leu Pro Lys Tyr Tyr Ile Leu Leu His Ile Met Leu Gly Glu Ile
 180 185 190
 Leu Arg His Ser Met Asp Pro Pro Thr Phe Thr Phe Asn Phe Asn Asn
 195 200 205
 Glu Pro Trp Val Arg Gly Arg His Glu Thr Tyr Leu Cys Tyr Glu Val
 210 215 220
 Glu Arg Met His Asn Asp Thr Trp Val Leu Leu Asn Gln Arg Arg Gly
 225 230 235 240
 Phe Leu Cys Asn Gln Ala Pro His Lys His Gly Phe Leu Glu Gly Arg
 245 250 255
 His Ala Glu Leu Cys Phe Leu Asp Val Ile Pro Phe Trp Lys Leu Asp
 260 265 270
 Leu Asp Gln Asp Tyr Arg Val Thr Cys Phe Thr Ser Trp Ser Pro Cys
 275 280 285
 Phe Ser Cys Ala Gln Glu Met Ala Lys Phe Ile Ser Lys Asn Lys His
 290 295 300
 Val Ser Leu Cys Ile Phe Thr Ala Arg Ile Tyr Asp Asp Gln Gly Arg
 305 310 315 320
 Cys Gln Glu Gly Leu Arg Thr Leu Ala Glu Ala Gly Ala Lys Ile Ser
 325 330 335
 Ile Met Thr Tyr Ser Glu Phe Lys His Cys Trp Asp Thr Phe Val Asp
 340 345 350
 His Gln Gly Cys Pro Phe Gln Pro Trp Asp Gly Leu Asp Glu His Ser
 355 360 365
 Gln Asp Leu Ser Gly Arg Leu Arg Ala Ile Leu Gln Asn Gln Glu Asn
 370 375 380

<210> 175

<211> 3005

<212> DNA

<213> Homo sapiens

<220>

<221> unsure

<222> (1407)

<400> 175

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gtggataaac aaaaagataa gaatggcgag agaattgatca caataagggg tggcacagaa 180
tcaacaagat atgcagttca actaatcaat gcactcattc aagatcctgc taaggaactg 240
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cttaataaga atgttccaac aaatgtacgt tcttctttcc cagtttctct acccttagct 480
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gtattaatgt gaaatattta ccagaatatt caataaaaaa atgaacagtc aaaaaaaaaa 3000
aaaaa 3005

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<210> 176
 <211> 832
 <212> PRT
 <213> Homo sapiens

<220>
 <221> UNSURE
 <222> (12)

<220>

128.

<221> UNSURE

<222> (449)

<400> 176

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Ala His Ile Asp Val Asp Lys Gln Lys Asp Lys Asn Gly Glu Arg Met
 20 25 30

Ile Thr Ile Arg Gly Gly Thr Glu Ser Thr Arg Tyr Ala Val Gln Leu
 35 40 45

Ile Asn Ala Leu Ile Gln Asp Pro Ala Lys Glu Leu Glu Asp Leu Ile
 50 55 60

Pro Lys Asn His Ile Arg Thr Pro Ala Ser Thr Lys Ser Ile His Ala
 65 70 75 80

Asn Phe Ser Ser Gly Val Gly Thr Thr Ala Ala Ser Ser Lys Asn Ala
 85 90 95

Phe Pro Leu Gly Ala Pro Thr Leu Val Thr Ser Gln Ala Thr Thr Leu
 100 105 110

Ser Thr Phe Gln Pro Ala Asn Lys Leu Asn Lys Asn Val Pro Thr Asn
 115 120 125

Val Arg Ser Ser Phe Pro Val Ser Leu Pro Leu Ala Tyr Pro His Pro
 130 135 140

His Phe Ala Leu Leu Ala Ala Gln Thr Met Gln Gln Ile Arg His Pro
 145 150 155 160

Arg Leu Pro Met Ala Gln Phe Gly Gly Thr Phe Ser Pro Ser Pro Asn
 165 170 175

Thr Trp Gly Pro Phe Pro Val Arg Pro Val Asn Pro Gly Asn Thr Asn
 180 185 190

Ser Ser Pro Lys His Asn Asn Thr Ser Arg Leu Pro Asn Gln Asn Gly
 195 200 205

Thr Val Leu Pro Ser Glu Ser Ala Gly Leu Ala Thr Ala Ser Cys Pro
 210 215 220

Ile Thr Val Ser Ser Val Val Ala Ala Ser Gln Gln Leu Cys Val Thr
 225 230 235 240

Asn Thr Arg Thr Pro Ser Ser Val Arg Lys Gln Leu Phe Ala Cys Val
 245 250 255

Pro Lys Thr Ser Pro Pro Ala Thr Val Ile Ser Ser Val Thr Ser Thr
 260 265 270

Cys Ser Ser Leu Pro Ser Val Ser Ser Ala Pro Ile Thr Ser Gly Gln
 275 280 285

Ala Pro Thr Thr Phe Leu Pro Ala Ser Thr Ser Gln Ala Gln Leu Ser
 290 295 300

Ser Gln Lys Met Glu Ser Phe Ser Ala Val Pro Pro Thr Lys Glu Lys
 305 310 315 320
 Val Ser Thr Gln Asp Gln Pro Met Ala Asn Leu Cys Thr Pro Ser Ser
 325 330 335
 Thr Ala Asn Ser Cys Ser Ser Ser Ala Ser Asn Thr Pro Gly Ala Pro
 340 345 350
 Glu Thr His Pro Ser Ser Ser Pro Thr Pro Thr Ser Ser Asn Thr Gln
 355 360 365
 Glu Glu Ala Gln Pro Ser Ser Val Ser Asp Leu Ser Pro Met Ser Met
 370 375 380
 Pro Phe Ala Ser Asn Ser Glu Pro Ala Pro Leu Thr Leu Thr Ser Pro
 385 390 395 400
 Arg Met Val Ala Ala Asp Asn Gln Asp Thr Ser Asn Leu Pro Gln Leu
 405 410 415
 Ala Val Pro Ala Pro Arg Val Ser His Arg Met Gln Pro Arg Gly Ser
 420 425 430
 Phe Tyr Ser Met Val Pro Asn Ala Thr Ile His Gln Asp Pro Gln Ser
 435 440 445
 Xaa Phe Val Thr Asn Pro Val Thr Leu Thr Pro Pro Gln Gly Pro Pro
 450 455 460
 Ala Ala Val Gln Leu Ser Ser Ala Val Asn Ile Met Asn Gly Ser Gln
 465 470 475 480
 Met His Ile Asn Pro Ala Asn Lys Ser Leu Pro Pro Thr Phe Gly Pro
 485 490 495
 Ala Thr Leu Phe Asn His Phe Ser Ser Leu Phe Asp Ser Ser Gln Val
 500 505 510
 Pro Ala Asn Gln Gly Trp Gly Asp Gly Pro Leu Ser Ser Arg Val Ala
 515 520 525
 Thr Asp Ala Ser Phe Thr Val Gln Ser Ala Phe Leu Gly Asn Ser Val
 530 535 540
 Leu Gly His Leu Glu Asn Met His Pro Asp Asn Ser Lys Ala Pro Gly
 545 550 555 560
 Phe Arg Pro Pro Ser Gln Arg Val Ser Thr Ser Pro Val Gly Leu Pro
 565 570 575
 Ser Ile Asp Pro Ser Gly Ser Ser Pro Ser Ser Ser Ser Ala Pro Leu
 580 585 590
 Ala Ser Phe Ser Gly Ile Pro Gly Thr Arg Val Phe Leu Gln Gly Pro
 595 600 605
 Ala Pro Val Gly Thr Pro Ser Phe Asn Arg Gln His Phe Ser Pro His
 610 615 620
 Pro Trp Thr Ser Ala Ser Asn Ser Ser Thr Ser Ala Pro Pro Thr Leu
 625 630 635 640

Gly Gln Pro Lys Gly Val Ser Ala Ser Gln Asp Arg Lys Ile Pro Pro
 645 650 655
 Pro Ile Gly Thr Glu Arg Leu Ala Arg Ile Arg Gln Gly Gly Ser Val
 660 665 670
 Ala Gln Ala Pro Ala Gly Thr Ser Phe Val Ala Pro Val Gly His Ser
 675 680 685
 Gly Ile Trp Ser Phe Gly Val Asn Ala Val Ser Glu Gly Leu Ser Gly
 690 695 700
 Trp Ser Gln Ser Val Met Gly Asn His Pro Met His Gln Gln Leu Ser
 705 710 715 720
 Asp Pro Ser Thr Phe Ser Gln His Gln Pro Met Glu Arg Asp Asp Ser
 725 730 735
 Gly Met Val Ala Pro Ser Asn Ile Phe His Gln Pro Met Ala Ser Gly
 740 745 750
 Phe Val Asp Phe Ser Lys Gly Leu Pro Ile Ser Met Tyr Gly Gly Thr
 755 760 765
 Ile Ile Pro Ser His Pro Gln Leu Ala Asp Val Pro Gly Gly Pro Leu
 770 775 780
 Phe Asn Gly Leu His Asn Pro Asp Pro Ala Trp Asn Pro Met Ile Lys
 785 790 795 800
 Val Ile Gln Asn Ser Thr Glu Cys Thr Asp Ala Gln Gln Ile Trp Pro
 805 810 815
 Gly Thr Trp Ala Pro His Ile Gly Asn Met His Leu Lys Tyr Val Asn
 820 825 830

<210> 177
 <211> 1561
 <212> DNA
 <213> Homo sapiens

<220>
 <221> unsure
 <222> (1150)

<400> 177
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 cctccctcgc ggctgggtga cagctgggtc cggctcgctc cgggctgcct ggggtgcgag 180
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 aggtgtaatt accccagaag agtttgtggc agctggagat cacctagtcc accactgtcc 540
 aacatggcaa tgggctacag gggaagaatt gaaagtgaag gcatacctac caacaggcaa 600
 acaatttttg gtaacaaaa atgtgccgtg ctataagcgg tgcaaacaga tggaatattc 660
 agatgaattg gaagctatca gtgaagaaga tgatgggtgat ggcggtatgg tagatacata 720
 tcacaacaca ggtattacag gaataacgga agccgttaaa gagatcacac tggaaaataa 780
 ggacaatata aggcttcaag attgctcagc actatgtgaa gaggaagaag atgaagatga 840

131

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aggagaagct gcagatatgg aagaatatga agagagtgga ttgttggaag cagatgaggc 900
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gactccaaga ttatggttgt ttggctatga tgagcaacgg cagcctttaa cagttgagca 1080
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tcatctgcn ccacctccca tgtgttcagt tcacccatgc aggcattgctg aggtgatgaa 1200
gaaaatcatt gagactgttg cagaaggagg gggagaactt ggagttcata tgtatcttct 1260
tattttcttg aaatttgtac aagctgtcat tccaacaata gaatatgact acacaagaca 1320
cttcacaatg taatgaagag agcataaaat ctatcctaatt tattggttct gatttttaaa 1380
gaattaaccc atagatgtga ccattgacca tattcatcaa tatatacagt ttctctaata 1440
agggacttat atgtttatgc attaaataaa aatatgttcc actaccagcc ttatttgttt 1500
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a                                                                                   1561

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<210> 178

<211> 314

<212> PRT

<213> Homo sapiens

<400> 178

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Met Gln Asn Val Ile Asn Thr Val Lys Gly Lys Ala Leu Glu Val Ala
  1                     5                     10                     15

```

```

Glu Tyr Leu Thr Pro Val Leu Lys Glu Ser Lys Phe Lys Glu Thr Gly
      20                     25                     30

```

```

Val Ile Thr Pro Glu Glu Phe Val Ala Ala Gly Asp His Leu Val His
      35                     40                     45

```

```

His Cys Pro Thr Trp Gln Trp Ala Thr Gly Glu Glu Leu Lys Val Lys
      50                     55                     60

```

```

Ala Tyr Leu Pro Thr Gly Lys Gln Phe Leu Val Thr Lys Asn Val Pro
      65                     70                     75                     80

```

```

Cys Tyr Lys Arg Cys Lys Gln Met Glu Tyr Ser Asp Glu Leu Glu Ala
      85                     90                     95

```

```

Ile Ser Glu Glu Asp Asp Gly Asp Gly Gly Trp Val Asp Thr Tyr His
      100                     105                     110

```

```

Asn Thr Gly Ile Thr Gly Ile Thr Glu Ala Val Lys Glu Ile Thr Leu
      115                     120                     125

```

```

Glu Asn Lys Asp Asn Ile Arg Leu Gln Asp Cys Ser Ala Leu Cys Glu
      130                     135                     140

```

```

Glu Glu Glu Asp Glu Asp Glu Gly Glu Ala Ala Asp Met Glu Glu Tyr
      145                     150                     155                     160

```

```

Glu Glu Ser Gly Leu Leu Glu Thr Asp Glu Ala Thr Leu Asp Thr Arg
      165                     170                     175

```

```

Lys Ile Val Glu Ala Cys Lys Ala Lys Thr Asp Ala Gly Gly Glu Asp
      180                     185                     190

```

```

Ala Ile Leu Gln Thr Arg Thr Tyr Asp Leu Tyr Ile Thr Tyr Asp Lys
      195                     200                     205

```

```

Tyr Tyr Gln Thr Pro Arg Leu Trp Leu Phe Gly Tyr Asp Glu Gln Arg
      210                     215                     220

```


132

Gln Pro Leu Thr Val Glu His Met Tyr Glu Asp Ile Ser Gln Asp His
225 230 235 240

Val Lys Lys Thr Val Thr Ile Glu Asn His Pro His Leu Pro Pro Pro
245 250 255

Pro Met Cys Ser Val His Pro Cys Arg His Ala Glu Val Met Lys Lys
260 265 270

Ile Ile Glu Thr Val Ala Glu Gly Gly Gly Glu Leu Gly Val His Met
275 280 285

Tyr Leu Leu Ile Phe Leu Lys Phe Val Gln Ala Val Ile Pro Thr Ile
290 295 300

Glu Tyr Asp Tyr Thr Arg His Phe Thr Met
305 310

<210> 179

<211> 2379

<212> DNA

<213> Homo sapiens

<400> 179

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ccatagttta aaatcgaata gtgccatcat cacagtatat tagtcaaata gaagcttcat 180
cagaaatgta tcccacatag agttttaaga cttggattct cttctgccct tgtaatctc 240
caactaatta ctacagattg acacgttttt aattagctgt cctttgtaag aagtcaggaa 300
atctgatgct gtgtccaaaa ttatgcactg tttgttgaag tagaaccaga aatcctgacc 360
tcctgttaaa tgacatcagt tccccctct gagcaacaga ctgcttgtct tgctaggaga 420
ggaggatggg gggctgagca ctcaggctgt ccattgaaac cccttgcca tgaatagggt 480
catactccta agactgatgg ggtgttgatc ttctaggaca tcacttgttt attcagtgcc 540
ccaaacacag atttctcttc tagcacttta gaattgatcc ttgaagtctc tcctggttca 600
ttcaaataca agctgtgtga gtctgggtgt ttctgtgat tggctctaat tgagctcttt 660
gaacagacag atctgacagt ggaatgactc tcccctgctt ctggcataac tgctttgctt 720
ctgtctagtg tccaagcatc ttagctgttc aagaggagag ggcagcataa cttcctgacc 780
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actcctgtaa tcccagcact ttgggaggcc cagtgaggtg ggagaattgc ttgaaccacag 2280
gaggcagagg ttgcagtgag ctgagattgc accattgcac tccagcctgg gtaacagagt 2340
gagactcctg tctcaaaaaa aaaaaaaaaa aaaaaaaaaa                2379

```

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<210> 180
<211> 67
<212> PRT
<213> Homo sapiens
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<400> 180
Met Gly Asp Trp Thr Trp Leu Tyr Arg Val Gly Cys Phe Phe Leu Ser
  1                               10                      15
Ala Ile Thr Cys His Ser Ile Leu Cys Ser Pro Arg Arg Met Val Ser
      20                               25                      30
Ala Phe Ser Cys Arg Cys Met Pro Ser Glu Pro Arg Asn Thr Lys Tyr
      35                               40                      45
Ile Gly Leu Lys Arg Glu Thr Gln Gly Cys Gln Phe Ser Val Gly Leu
  50                               55                      60

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Pro Leu Pro
65

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<210> 181
<211> 1607
<212> DNA
<213> Homo sapiens
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<400>	181						
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taacgatgaa	ccattttaaa	ggggagggtta	tttgaaacct	ctaatttgat	tattggggagg	120	
attttcatgc	tttcttttagt	atttattacc	atcataccga	ttcaaactat	tttattgtct	180	
aatacattag	catttttgat	tttgatggaa	attgttacag	aatttaaaga	tttgatgaaa	240	
taagatgtag	cagatttttt	gtagcaagtt	tctggtaaaa	gggtttttttg	caagtctcag	300	
gttctgtctg	cactattttt	ttttaaatat	tattccagt	tattctaatt	cagaagcatt	360	
cttttcaagt	aacagcagca	cttgtgaaaag	gaaaaaaaaa	tgccatgttt	tcttagtagg	420	
ttactaaaatt	tgtacaatta	attaagattt	tagccatcag	tgagtttgaa	aaggggaaatg	480	
tatttattttt	cagcattaaa	atgcttccaa	aagatcaagt	tgcttttggt	tgtttggttt	540	
tttaaccgta	atgtagatgg	agaaattgga	ggcaacctca	gtataggaac	tgccactttg	600	
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attgtacca	ctcctctggc	ctcctctccc	tcaattaaaa	aaacacactt	accagttttg	720	
cttatttttac	agatatctgg	tggttctata	gtttaaagca	gcttgtgaaa	ttaaaaaagt	780	
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aattatttta	tttttgaaatt	ctggaatttg	aacatttact	gtaattttgta	atataactgc	1560	
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<210> 182
<211> 58
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<212> PRT

<213> Homo sapiens

<400> 182

Met Tyr Leu Phe Ser Ala Leu Lys Cys Phe Gln Lys Ile Lys Leu Leu
 1 5 10 15

Leu Phe Val Cys Phe Phe Asn Arg Asn Val Asp Gly Glu Ile Gly Gly
 20 25 30

Asn Leu Ser Ile Gly Thr Ala Thr Leu Ser Ser Leu Gly Leu Lys Glu
 35 40 45

Lys Val Asn Leu Met Pro Arg Gly Glu Gln
 50 55

<210> 183

<211> 2695

<212> DNA

<213> Homo sapiens

<400> 183

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 ctatgtgagt gtactcagag tccaggggca aggtagtcac cctgtgtgtg gtgggaaaaat 180
 actgcaagat tataatgtcaa ataatgggat actcaggaat atttacaaaa atgttgaata 240
 ttttaattgaa ataacaaata ttttagacatt caatagactt gagagtaact ttaccaaggy 300
 tctaagtatg agagatatgt ttaatatatt tttatgggct gaaaaccctg agtgggaaaa 360
 taggactaat ttcaccagga tgacctcctg gaaatgcatt ttccattttg gaaattattt 420
 taaaagttca ttttttctgg atgggtatgt gtatgtgtgt gtgtctgtcy aygtgtgtat 480
 gttttatgag cttgttaaca ctaatgtcat acaaaagtac tggttagcag gaataagatt 540
 ttaaggtgta ttggcattcc catggttccc aagaaaattt tagatgactt tgattaaaaa 600
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 taacaaacag ctaaagttac tgaacacaaa ttatggaaag gtgaaatgag gaaaacattg 780
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135

aagccatgtg tattcacaat acagttcata ttatcatgtt tcatttgaaa aatttatgat 2400
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<210> 184

<211> 256

<212> PRT

<213> Homo sapiens

<220>

<221> UNSURE

<222> (64)

<400> 184

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 20 25 30
 Ile Glu Trp Val Lys Arg Gln Lys Ile Ser Phe Ala Asp Gln Ile Leu
 35 40 45
 Thr Ala Leu Ala Val Ser Arg Val Gly Leu Leu Trp Val Ile Leu Xaa
 50 55 60
 His Trp Tyr Ala Thr Val Leu Asn Pro Gly Ser Tyr Ser Leu Gly Val
 65 70 75 80
 Arg Ile Thr Thr Ile Asn Ala Trp Ala Val Thr Asn His Phe Ser Ile
 85 90 95
 Trp Val Ala Thr Ser Leu Ser Ile Phe Tyr Leu Leu Lys Ile Ala Asn
 100 105 110
 Phe Ser Asn Phe Ile Phe Leu His Leu Lys Arg Arg Ile Lys Ser Val
 115 120 125
 Ile Pro Val Ile Leu Leu Gly Ser Leu Leu Phe Leu Val Cys His Leu
 130 135 140
 Val Val Val Asn Met Asp Glu Ser Met Trp Thr Lys Glu Tyr Glu Gly
 145 150 155 160
 Asn Val Ser Trp Glu Ile Lys Leu Ser Asp Pro Thr His Leu Ser Asp
 165 170 175
 Met Thr Val Thr Thr Leu Ala Asn Leu Ile Pro Phe Thr Leu Ser Leu
 180 185 190
 Leu Ser Phe Leu Leu Leu Ile Cys Ser Leu Cys Lys His Leu Lys Lys
 195 200 205
 Met Gln Phe His Gly Lys Gly Ser Pro Asp Ser Asn Thr Lys Val His
 210 215 220
 Ile Lys Ala Leu Gln Thr Val Thr Ser Phe Leu Leu Leu Phe Ala Val
 225 230 235 240

136.

Tyr Phe Leu Ser Leu Ile Thr Ser Ile Trp Asn Phe Arg Arg Arg Leu
 245 250 255

<210> 185
 <211> 1111
 <212> DNA
 <213> Homo sapiens

<400> 185
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 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 1111

<210> 186
 <211> 290
 <212> PRT
 <213> Homo sapiens

<400> 186
 Met Tyr His Gly Met Asn Pro Ser Asn Gly Asp Gly Phe Leu Glu Gln
 1 5 10 15
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 20 25 30
 Ile Leu Trp Phe Gln Leu Ala Leu Cys Phe Gly Pro Ala Gln Leu Thr
 35 40 45
 Gly Gly Phe Asp Asp Leu Gln Val Cys Ala Asp Pro Gly Ile Pro Glu
 50 55 60
 Asn Gly Phe Arg Thr Pro Ser Gly Gly Val Phe Phe Glu Gly Ser Val
 65 70 75 80
 Ala Arg Phe His Cys Gln Asp Gly Phe Lys Leu Lys Gly Ala Thr Lys
 85 90 95
 Arg Leu Cys Leu Lys His Phe Asn Gly Thr Leu Gly Trp Ile Pro Ser
 100 105 110
 Asp Asn Ser Ile Cys Val Gln Glu Asp Cys Arg Ile Pro Gln Ile Glu
 115 120 125
 Asp Ala Glu Ile His Asn Lys Thr Tyr Arg His Gly Glu Lys Leu Ile
 130 135 140

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Ile Thr Cys His Glu Gly Phe Lys Ile Arg Tyr Pro Asp Leu His Asn
 145 150 155 160
 Met Val Ser Leu Cys Arg Asp Asp Gly Thr Trp Asn Asn Leu Pro Ile
 165 170 175
 Cys Gln Gly Cys Leu Arg Pro Leu Ala Ser Ser Asn Gly Tyr Val Asn
 180 185 190
 Ile Ser Glu Leu Gln Thr Ser Phe Pro Val Gly Thr Val Ile Ser Tyr
 195 200 205
 Arg Cys Phe Pro Gly Phe Lys Leu Asp Gly Ser Ala Tyr Leu Glu Cys
 210 215 220
 Leu Gln Asn Leu Ile Trp Ser Ser Ser Pro Pro Arg Cys Leu Ala Leu
 225 230 235 240
 Glu Gly Gly Arg Pro Glu His Leu Phe Pro Val Leu Tyr Phe Pro His
 245 250 255
 Ile Arg Leu Ala Ala Ala Val Leu Tyr Phe Cys Pro Val Leu Lys Ser
 260 265 270
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 275 280 285
 Leu Phe
 290

<210> 187
 <211> 29
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> oligonucleotide

<220>
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 <222> (2)
 <223> biotinylated phosphoramidite residue

<400> 187
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29

<210> 188
 <211> 29
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> oligonucleotide

<220>
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 <222> (2)
 <223> biotinylated phosphoramidite residue

<400> 188

tncagaaaga ctgcagggat tcgggacaa 29

<210> 189
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<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide

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<400> 189
antcatcact acacgtcttc tcccctaca 29

<210> 190
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<213> Artificial Sequence

<220>
<223> oligonucleotide

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<222> (2)
<223> biotinylated phosphoramidite residue

<400> 190
gnctgagtat gttgtggaat gggctgcaa 29

<210> 191
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> oligonucleotide

<220>
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<222> (2)
<223> biotinylated phosphoramidite residue

<400> 191
tngtgactgt atacctgcaa cctcaatgc 29

<210> 192
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<400> 195
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<400> 196
ctgccactat ccccaggg 18

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<400> 200
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29

<210> 201
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29

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<400> 202
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142

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29

<210> 205
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29

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<400> 206
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<400> 208
tcctcaccct cttcccttg

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144

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<400> 212
ggtatgggaa gctagagggc 20

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gtctgggacg atgttggc 18

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<400> 215
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29

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<400> 219

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29

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<400> 222

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29

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29

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29

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<210> 227
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148

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29

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<400> 235

gtttctggaa tgcgggtg

18

<210> 236

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<400> 236

ccgtgatacc gaaatgtcc

19

<210> 237

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<400> 237

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29

<210> 238

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29

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29

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29

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29

<210> 242

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<400> 244
ggctctacat ctcacacccc

20

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29

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cnaatccatgg tacatgggtca gaagctcat

29

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<400> 248
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<210> 252
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<400> 252
cngtcagggc gcagctgtat tggtcacaa 29

<210> 253
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<400> 253
acccacacag aagtgagcc 19

<210> 254
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<400> 255
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<400> 257
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<400> 258
ttggagcact gaggaacaag 20

<210> 259
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<400> 259

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29

<210> 260

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<400> 260

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29

<210> 261

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<400> 262

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29

<210> 263

<211> 29

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<400> 263
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29

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<400> 264
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29

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29

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<400> 266
gngctgggag tactgctaga ggggtgtgga

29

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<223> biotinylated phosphoramidite residue

<400> 267
cncctctttgg ctgtacacga acttgctcc 29

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<400> 268
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<213> Artificial Sequence

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<400> 270
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<210> 271
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<212> DNA
<213> Artificial Sequence

159

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<220>
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<400> 271
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 gntacatctt tcatccacag agggcatcc 29

<210> 274
 <211> 51
 <212> PRT
 <213> Homo sapiens

<400> 274
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 1 5 10 15

Pro Ser Leu Asp Val Cys Thr Asn Tyr Ser Leu Glu Leu Phe Ser Leu
 20 25 30

Ala Leu Gln Leu Leu Pro Pro Thr Ser Ser Pro Ala Pro Pro Ile His
 35 40 45

Ser Phe Ala
 50

160

<210> 275
 <211> 82
 <212> PRT
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<220>
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 Gly Ser Gly Pro Ser Gly Trp Cys Leu Gln Gly Asn Phe Gly Pro Ser
 20 25 30
 Leu Phe Ser Asp Trp Arg Ser Pro Trp Pro Ala Ser Phe His Thr Xaa
 35 40 45
 Leu Leu Ala Gly Thr Gly Leu Ala Pro Thr Phe Pro Ala Ser Ser Val
 50 55 60
 Val Ala Ser Leu Pro Glu Pro Gly Ser Ser Ser Gly Pro Thr Ser Lys
 65 70 75 80
 Cys His

<210> 276
 <211> 130
 <212> PRT
 <213> Homo sapiens

<400> 276
 Met Asp Asp Met Leu Ser Thr Arg Ser Ser Thr Leu Thr Glu Asp Gly
 1 5 10 15
 Ala Lys Ser Ser Glu Ala Ile Lys Glu Ser Ser Lys Phe Pro Phe Gly
 20 25 30
 Ile Ser Pro Ala Gln Ser His Arg Asn Ile Lys Ile Leu Glu Asp Glu
 35 40 45
 Pro His Ser Lys Asp Glu Thr Pro Leu Cys Thr Leu Leu Asp Trp Gln
 50 55 60
 Asp Ser Leu Ala Lys Arg Cys Val Cys Val Ser Asn Thr Ile Arg Ser
 65 70 75 80
 Leu Ser Phe Val Pro Gly Asn Asp Phe Glu Met Ser Lys His Pro Gly
 85 90 95
 Leu Leu Leu Ile Leu Gly Lys Leu Ile Leu Leu His Lys His Pro
 100 105 110
 Glu Arg Lys Gln Ala Pro Leu Thr Tyr Glu Lys Glu Glu Glu Gln Asp
 115 120 125
 Gln Gly
 130

161

<210> 277

<211> 111

<212> PRT

<213> Homo sapiens

<400> 277

Met Leu Gly Tyr Arg Lys Ile Asn Ala Lys Ala Lys His Pro Val Pro
 1 5 10 15

Val Leu Glu Val Pro Arg Gly Arg Met Pro Arg Leu Arg Lys Lys Leu
 20 25 30

Leu Ser Trp Pro Gly Gln Arg Glu Glu Glu Pro Arg Val Gly Val Val
 35 40 45

Thr His Leu Lys Ile Thr Met Ser Ser Gly Arg Cys Ala Ile Val Leu
 50 55 60

Gly Leu Gly Gly Cys Gly Arg Pro Thr Leu Gly Met Gln Ser Ser Asp
 65 70 75 80

Ser Val Ser Leu Ala Thr Leu Gly Leu Leu Thr Thr Leu Pro Val Leu
 85 90 95

Leu Thr Leu Arg Glu Gly Ser Cys Trp Val Asp Ser Arg Gln Ala
 100 105 110

<210> 278

<211> 104

<212> PRT

<213> Homo sapiens

<400> 278

Met Glu Asn Ser Leu Leu Ala Met Phe His Glu Ser Arg Ile Leu His
 1 5 10 15

Leu Trp Ala Ala Leu Phe Leu Val Glu Leu Leu Gln Glu Val Pro Ile
 20 25 30

Met Thr Cys Ser Asn Ala Asn Thr Pro Ser Val Asn Thr Gly Tyr Phe
 35 40 45

Lys Leu Ser Ser Val Ala Thr Thr Leu Arg Gln Gln Gln Leu Val Leu
 50 55 60

Glu Ile Ser Leu Met Ser Val Pro Pro Gly Cys Gly Pro Leu Leu Pro
 65 70 75 80

Val Leu Ile Pro Val Ala Ser Phe Cys Cys Ile Ile Thr Ile Trp Leu
 85 90 95

Leu Ile Leu Met Phe Glu Lys Asp
 100

<210> 279

<211> 147

<212> PRT

<213> Homo sapiens

162.

<400> 279

Met Ala Ser Pro Ser Gly Leu Cys Val Leu Val Arg Leu Pro Lys Leu
 1 5 10 15

Ile Cys Gly Gly Lys Thr Leu Pro Arg Thr Leu Leu Asp Ile Leu Ala
 20 25 30

Asp Gly Thr Ile Leu Lys Val Gly Val Gly Cys Ser Glu Asp Ala Ser
 35 40 45

Lys Leu Leu Gln Asp Tyr Gly Leu Val Val Arg Gly Cys Leu Asp Leu
 50 55 60

Arg Tyr Leu Ala Met Arg Gln Arg Asn Asn Leu Leu Cys Asn Gly Leu
 65 70 75 80

Ser Leu Lys Ser Leu Ala Glu Thr Val Leu Asn Phe Pro Leu Asp Lys
 85 90 95

Ser Leu Leu Leu Arg Cys Ser Asn Trp Asp Ala Glu Thr Leu Thr Glu
 100 105 110

Asp Gln Val Ile Tyr Ala Ala Arg Asp Ala Gln Ile Ser Val Ala Leu
 115 120 125

Phe Leu His Leu Leu Gly Tyr Pro Phe Ser Arg Asn Ser Pro Gly Glu
 130 135 140

Lys Lys Arg
 145

<210> 280

<211> 176

<212> PRT

<213> Homo sapiens

<400> 280

Met Thr Asp Cys Leu Val Ile Lys His Phe Leu Arg Lys Ile Ile Met
 1 5 10 15

Val His Pro Lys Val Arg Phe His Phe Ser Val Lys Val Asn Gly Ile
 20 25 30

Leu Ser Thr Glu Ile Phe Gly Val Glu Asn Glu Pro Thr Leu Asn Leu
 35 40 45

Gly Asn Gly Ile Ala Leu Leu Val Asp Ser Gln His Tyr Val Ser Arg
 50 55 60

Pro Asn Phe Gly Thr Ile Glu Ser His Cys Ser Arg Ile His Pro Val
 65 70 75 80

Leu Gly His Pro Val Met Leu Phe Ile Pro Glu Asp Val Ala Gly Met
 85 90 95

Asp Leu Leu Gly Glu Leu Ile Leu Thr Pro Ala Ala Ala Leu Cys Pro
 100 105 110

Ser Pro Lys Val Ser Ser Asn Gln Leu Asn Arg Ile Ser Ser Val Ser
 115 120 125

163

Ile Phe Leu Tyr Gly Pro Leu Gly Leu Pro Leu Ile Leu Ser Thr Trp
 130 135 140

Glu Gln Pro Met Thr Thr Phe Phe Lys Asp Thr Ser Ser Leu Val Asp
 145 150 155 160

Trp Lys Ile Pro Phe Val Tyr Asp Thr Gln Phe Gly Ser Gln Phe Gly
 165 170 175

<210> 281

<211> 89

<212> PRT

<213> Homo sapiens

<400> 281

Met Gly Ser Leu Ser Thr Ala Asn Val Glu Phe Cys Leu Asp Val Phe
 1 5 10 15

Lys Glu Leu Asn Ser Asn Asn Ile Gly Asp Asn Ile Phe Phe Ser Ser
 20 25 30

Leu Ser Leu Leu Tyr Ala Leu Ser Met Val Leu Leu Gly Ala Arg Gly
 35 40 45

Glu Thr Ala Glu Gln Leu Glu Lys Val Leu His Phe Ser His Thr Val
 50 55 60

Asp Ser Leu Lys Pro Gly Phe Lys Asp Ser Pro Lys Cys Ser Gln Ala
 65 70 75 80

Gly Arg Ile His Ser Glu Phe Gly Val
 85

<210> 282

<211> 115

<212> PRT

<213> Homo sapiens

<400> 282

Met Val Thr Gly Met Leu Ile Ser Ser Thr Arg Gly Ser Ser Asp Gly
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Arg Asn Cys Ser Ala Ile Leu Val Pro Val Ser Pro Val Gly Arg Gln
 20 25 30

Pro Leu Tyr Leu Thr Ser Arg Pro Gly Asp Trp Ser Gln Gly Tyr Cys
 35 40 45

Thr Thr Gly Gln Phe Pro Ala Ile Val Arg Lys Glu Thr Pro Glu Leu
 50 55 60

Asn Gly Arg Asp Ile Pro Ala Val Phe Asn Ile Thr Pro Met Pro Phe
 65 70 75 80

Val Arg Leu Pro Cys Thr Glu Ile Thr Trp Arg Ala Ser Cys Arg Leu
 85 90 95

Tyr Leu Arg Thr Leu Val Lys Tyr Leu Leu Ser Phe Leu Ala Ala Arg
 100 105 110

164

Met Gln Lys
115

<210> 283

<211> 189

<212> PRT

<213> Homo sapiens

<400> 283

Met Val His Cys Pro His Glu Leu Leu Gln Met Pro Leu Ser Leu Phe
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Ser Gln Arg Ser Trp Val Thr Gln Cys Leu Asp Thr Trp Lys Thr Cys
20 25 30

Thr Leu Ile Thr Gln Arg His Leu Ala Ser Asp His Leu Pro Ser Glu
35 40 45

Phe Leu Leu Val Gln Leu Gly Tyr His Pro Leu Thr His Gln Ala Ala
50 55 60

Pro His Leu Pro Leu Leu Leu Leu Trp Gln Val Phe Pro Ala Tyr Gln
65 70 75 80

Glu Gln Gly Phe Ser Cys Lys Gly Gln Leu Leu Leu Gly Leu Leu Val
85 90 95

Ser Thr Asp Asn Ile Phe Leu Pro Ile Leu Gly Gln Ala Pro Gln Thr
100 105 110

His Pro Leu Leu Pro His Gln Arg Trp Ala Asn Gln Lys Glu Ser Val
115 120 125

Pro Val Lys Ile Glu Arg Tyr Leu Pro Gln Leu Glu Gln Arg Asp Trp
130 135 140

Pro Glu Phe Gly Lys Glu Gly Leu Leu His Lys Pro Arg Arg Gly Pro
145 150 155 160

Val Leu Ser Leu Pro Leu Asp Thr Val Glu Ser Gly His Leu Val Ser
165 170 175

Met Leu Cys Gln Lys Ala Tyr Gln Val Gly Arg Asn Leu
180 185

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HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,
MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,
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patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,
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*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
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WO 01/075068 A3

(54) Title: SECRETED PROTEINS AND POLYNUCLEOTIDES ENCODING THEM

(57) Abstract: Novel polynucleotides and the proteins encoded thereby are disclosed.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/09369

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :Please See Extra Sheet.

US CL :Please See Extra Sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : *Please See Extra Sheet*

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Database: N_Geneseq_1101; Accession NO: AAX60801; Agostino et al., "Human secreted protein encoding DNA (clone bd306_7)"; 09 August 1999; having 100% sequence identity to SEQ ID NO: 1; see entire document.	1, 2, 7, 8
X	Database: A_Geneseq_1101; Accession NO: AAY17219; Agostino et al.; "Human secreted protein (clone bd306_7); 09 August 1999; having 99.9% sequence identity to SEQ ID NO: 2; see entire document.	1, 2, 7, 8

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search 07 JUNE 2002	Date of mailing of the international search report 02 JUL 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer RITA MITRA Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/09369

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99/26961 A1 (GENETICS INSTITUTE, INC) 03 JUNE 1999,see entire document,especially pages 51 and 57.	1-5, 7, 8
X	Database: SPTREMBL_17; Accession NO: O75718; Castagnola et al. " Cartilage-associated protein (CASP) precursor"; 01 November 1998; having 99.9% sequence identity to SEQ ID NO: 2; see entire document.	1, 2, 7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/09369

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-5, 7, 8

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/09369

A. CLASSIFICATION OF SUBJECT MATTER:

IPC (7):

C07H 21/02, 21/04; C07K 5/00, 14/00; C12Q 1/68; C12P 21/06, C12N 1/20, 15/63, 5/00

A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

536/23.1, 23.5, 24.31; 530/300, 350; 435/6, 69.1, 252.3, 320.1, 325

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

Sequence Search (Database: GenEmbl, N_Geneseq_1101, Issued_Patents_NA, EST, A_Geneseq_1101, Issued_Patents_AA, Pir_6,8 SwissProt_39, SPTREMBL_17)

STN (Database: CA, CAPLUS, USPATFULL)

DIALOG (Database: MEDLINE, BIOSIS, DIALOG GLOBAL REPORTER, DERWENT WPI)

Search Terms: polynucleotide, polypeptide, secreted protein, transmembrane protein

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I. Claims 1-5, 7, 8, directed to an isolated polynucleotide comprising or related to nucleotide sequence of SEQ ID NO: 1 that encodes a protein of SEQ ID NO: 2, vector, host cell and a process of producing the protein recombinantly.

Group II. Claims 6, 9-12, directed to an isolated protein comprising or related to amino acid sequence of SEQ ID NO: 2, a composition comprising the protein related to SEQ ID NO: 2.

Group III. Claim 13, directed to an isolated polynucleotide comprising or related to the nucleotide sequence of SEQ ID NO: 19.

Group IV. Claim 14, directed to an isolated protein comprising or related to amino acid sequence of SEQ ID NO: 20.

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I-IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The polynucleotides and polypeptides of each of the clones bd306_7 and ybd_1 in the claims are unrelated, each to the other. The polynucleotide sequences encode structurally distinct polypeptides and do not share a special technical feature. Furthermore, the technical feature that links the DNA, protein, methods of cDNA clone bd306_7 (claim 1) is not a contribution over the prior arts of Agostino et al. and Castagnola et al. See the various documents cited in the search report. Thus the technical feature of the polynucleotide sequence is not special and the groups are not so linked under PCT Rule 13.1. Additionally the claimed methods produce different products and/or different results which are not coextensive and which do not share the same technical feature.